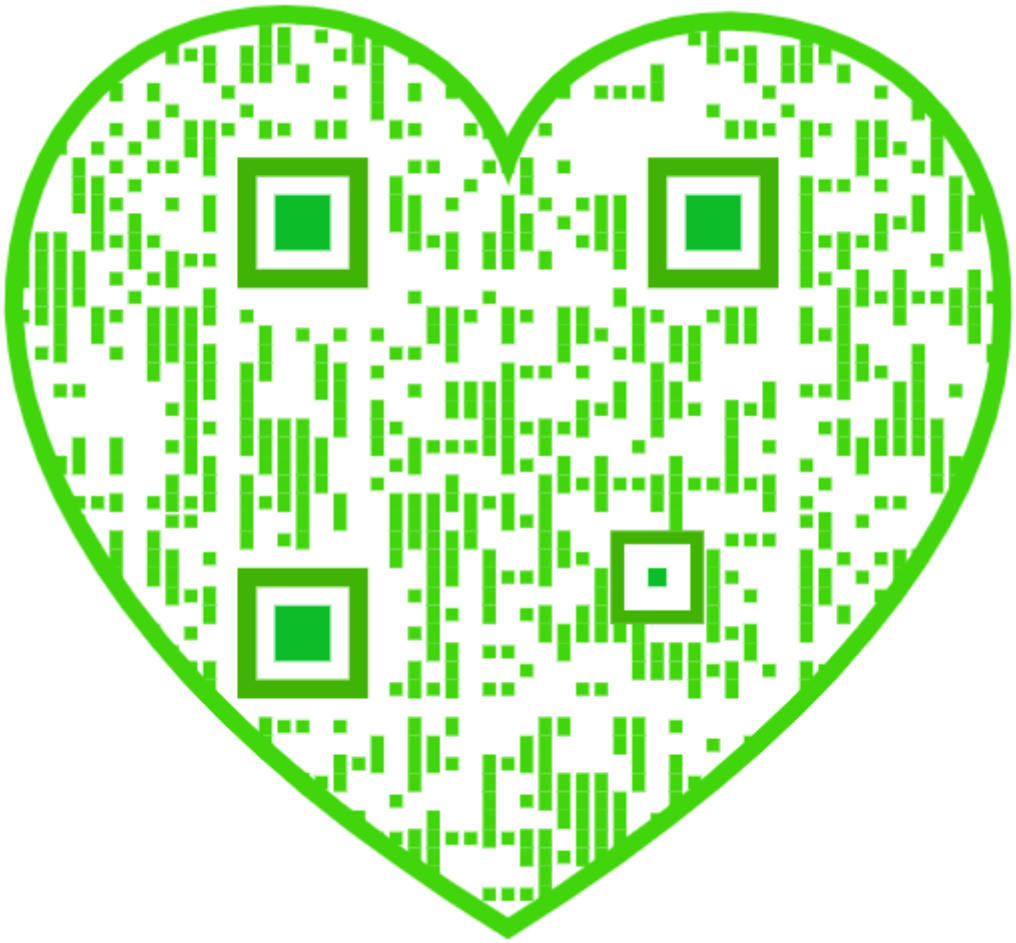
HHS Pandemic Influenza Plan

U.S. Department of Health and Human Services

November 2005



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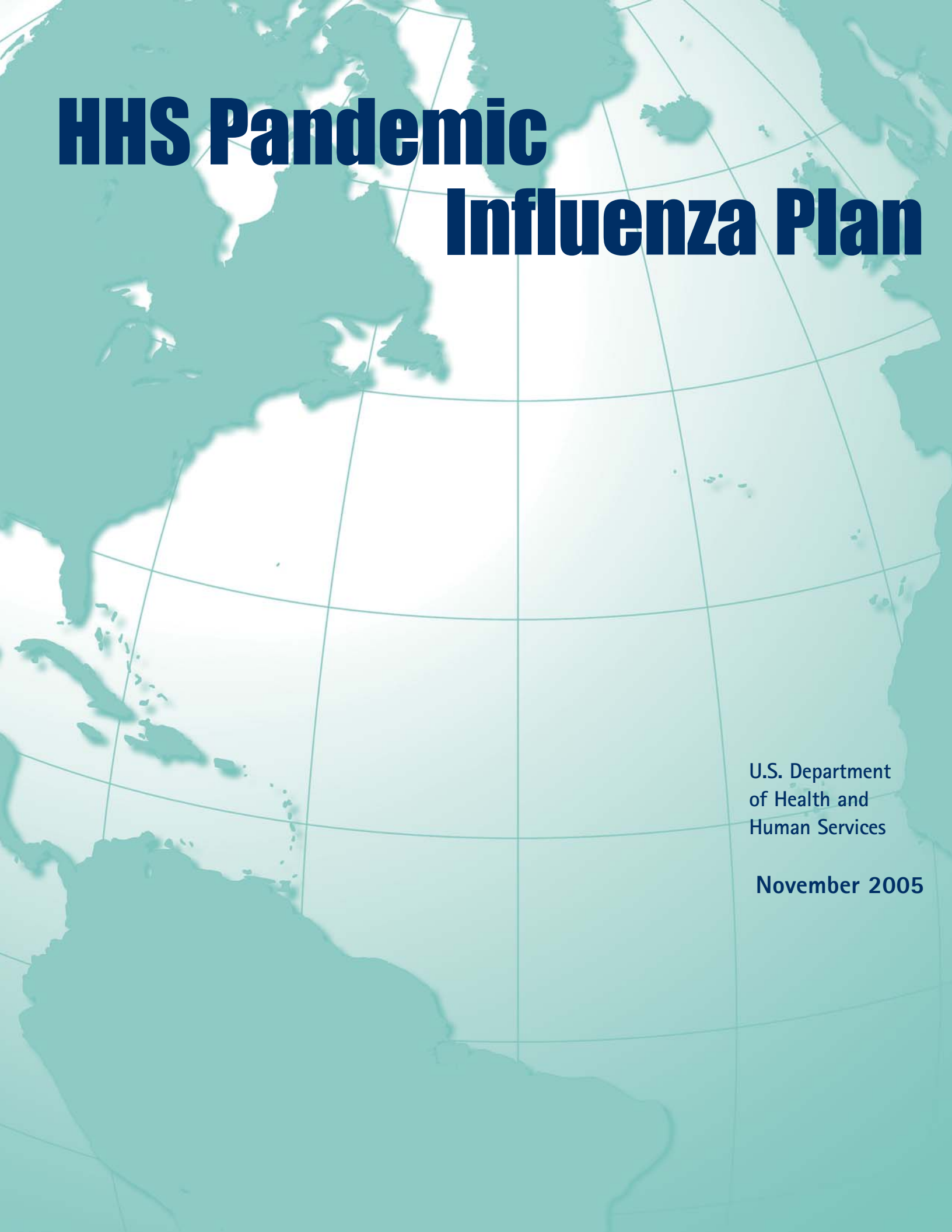

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Statement by Health and Human Services Secretary Mike Leavitt:

One of the most important public health issues our Nation and the world faces is the threat of a global disease outbreak called a pandemic. No one in the world today is fully prepared for a pandemic -- but we are better prepared today than we were yesterday - and we will be better prepared tomorrow than we are today.

This *HHS Pandemic Influenza Plan* provides a blueprint from which to prepare for the challenges that lie ahead of us. Being prepared and responding effectively involves everyone: individuals, communities, businesses, States, Federal agencies, international countries and organizations. Here at home, we can use this *Plan* to create a seamless preparedness network where we are all working together for the benefit of the American people.

In the century past, we have experienced influenza pandemics three times: as recently as 1968 and 1957 and what has been called the Great Influenza in 1918, a pandemic that killed 40-50 million people worldwide. At some point in our nation's future another virus will emerge with the potential to create a global disease outbreak. History teaches us that everything we do today to prepare for that eventuality will have many lasting benefits for the future. We will realize important advances in healthcare, and we will be better prepared for other types of emergencies.

I am humbled by the enormity of the challenge that the global community confronts should there be a pandemic. Public cooperation and global partnerships will be essential tools in fighting back and creating a constant state of readiness. If together we take the steps necessary, we will be able to save the lives of millions of people in our country and all around the world.

Mike Leavitt
Health and Human Services Secretary

preface

Adequate planning for a pandemic requires the involvement of every level of our nation, and indeed, the world. The ubiquitous nature of an influenza pandemic compels federal, state and local governments, communities, corporations, families and individuals to learn about, prepare for, and collaborate in efforts to slow, respond to, mitigate, and recover from a potential pandemic. The development, refinement, and exercise of pandemic influenza plans by all stakeholders are critical components of preparedness.

This document, the **HHS Pandemic Influenza Plan**, serves as a blueprint for all HHS pandemic influenza preparedness planning and response activities. This plan updates the August 2004 draft HHS Pandemic Influenza Preparedness and Response Plan and features important additions and refinements. The Plan integrates changes made in the 2005 World Health Organization (WHO) classification of pandemic phases and expansion of international guidance and now is consistent with the National Response Plan (NRP) published in December 2004.

The **HHS Pandemic Influenza Plan** has three parts, the first two of which are contained in this document. Part 1, the **Strategic Plan** outlines federal plans and preparation for public health and medical support in the event of a pandemic. It identifies key roles of HHS and its agencies in a pandemic and provides planning assumptions for federal, state and local governments and public health operations plans. Part 2, **Public Health Guidance for State and Local Partners**, provides detailed guidance to state and local health departments in 11 key areas. Parts 1 and 2 will be regularly updated and refined. These documents will serve as tools for continued engagement with stakeholders, state and local partners.

Part 3, which is currently under development, will consist of **HHS Agencies' Operational Plans**. Each HHS component will prepare, maintain, update and exercise an operational plan that itemizes their specific roles and responsibilities in the event of a pandemic. These individual plans will also include detailed continuity of operations plans such as strategies for ensuring that critical everyday functions of each operating division are identified and maintained in the presence of the expected decreased staffing levels of a pandemic event. In addition to operations, these plans will elaborate on coordination, command and control, logistics, and planning, as well as financial and administration considerations.

Recognizing that an influenza pandemic has the capacity to cause disruptions across all levels of governments and in all communities, pandemic influenza preparedness is a shared responsibility. The following list includes some of the additional plans that will be required to mitigate the impact of a pandemic and to ensure continuity of essential services:

All plans should remain living documents. They should be updated periodically in the time before, during, and after a pandemic. All plans should be exercised to identify weaknesses and promote effective implementation.

International and Global Planning

Every nation should develop comprehensive strategies and contingency plans for a global pandemic. These plans should be coordinated regionally and at the global level. The opportunity to contain an initial outbreak can only be realized in the presence of a sophisticated global strategy.

National Strategy for Pandemic Influenza

The National Strategy provides a framework for future U.S. Government planning efforts. It acknowledges that the Nation must have a system of plans at all levels of government and in all sectors outside of government, that can be integrated to address the pandemic threat.

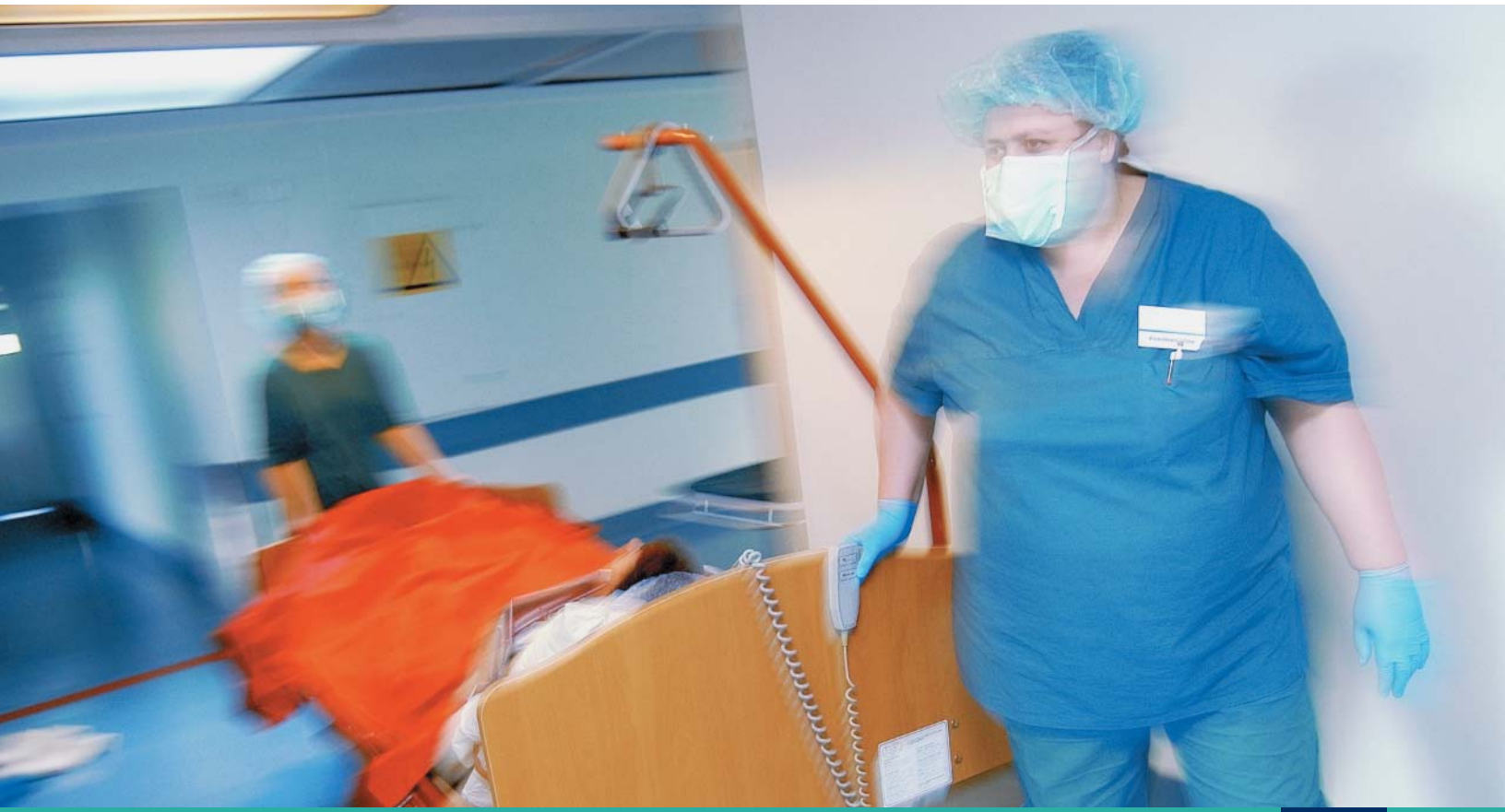
State and Local Pandemic Influenza Plans

These plans should detail how health departments and other agencies of state and local governments and tribal nations will prevent, mitigate, respond and recover from an influenza pandemic. They should be community specific where appropriate and should contemplate specific local and community needs.

Corporate, Infrastructure and Critical Service Provider Plans

School systems, hospitals, healthcare providers, community infrastructure providers and employers should develop plans that identify how they will respond in the event of an influenza pandemic.

All plans should remain living documents. They should be updated periodically in the time before, during, and after a pandemic. All plans should be exercised to identify weaknesses and promote effective implementation. Pandemic influenza response can be optimized by effectively engaging stakeholders during all phases of pandemic planning and response.



Although the timing, nature and severity of the next pandemic cannot be predicted with any certainty, preparedness planning is imperative to lessen the impact of a pandemic.

executive summary

An influenza pandemic has the potential to cause more death and illness than any other public health threat. If a pandemic influenza virus with similar virulence to the 1918 strain emerged today, in the absence of intervention, it is estimated that 1.9 million Americans could die and almost 10 million could be hospitalized over the course of the pandemic, which may evolve over a year or more. Although the timing, nature and severity of the next pandemic cannot be predicted with any certainty, preparedness planning is imperative to lessen the impact of a pandemic. The unique characteristics and events of a pandemic will strain local, state, and federal resources. It is unlikely that there will be sufficient personnel, equipment, and supplies to respond adequately to multiple areas of the country for a sustained period of time. Therefore, minimizing social and economic disruption will require a coordinated response. Governments, communities, and other public and private sector stakeholders will need to anticipate and prepare for a pandemic by defining roles and responsibilities and developing continuity of operations plans.

This document, the **HHS Pandemic Influenza Plan**, serves as a blueprint for all HHS pandemic influenza preparedness and response planning. Part 1, the **Strategic Plan**, describes a coordinated public health and medical care strategy to prepare for, and begin responding to, an influenza pandemic. Part 2, **Public Health Guidance for State and Local Partners** provides guidance on specific aspects of pandemic influenza planning and response for the development of state and local preparedness plans.

Part 1 – Strategic Plan

Part 1 describes the pandemic influenza threat and outlines planning assumptions and doctrine for the HHS pandemic influenza response. In addition, it identifies key pandemic response actions and the necessary capabilities for effective implementation. Finally, the **Strategic Plan** assigns lead roles and responsibilities for response actions to specific HHS agencies and offices.

The Pandemic Influenza Threat

A pandemic occurs when a novel influenza virus emerges that can infect and be efficiently transmitted among individuals because of a lack of pre-existing immunity in the population. The extent and severity of a pandemic depends on the specific characteristics of the virus.

Although a novel influenza virus could emerge from anywhere in the world at any time, scientists are particularly concerned about the avian influenza (H5N1) currently circulating in Asia and parts of Europe.

Outbreaks of influenza H5N1 have occurred among poultry in several countries in Asia since 1997. The H5N1 avian influenza virus is widespread in the region and has become endemic in migratory birds and several other animal species. As of October 2005, cases of human H5N1 infection have been reported in Thailand, Vietnam, Cambodia, and Indonesia. The reported death rate for these cases has been about 50 percent, although the true number of people who have been exposed to and infected by the H5N1 virus is unknown. While most of the reported cases seem to have occurred from direct contact with infected poultry or contaminated surfaces, the source of infection has not been documented in every instance. Of additional concern are the few instances where secondary transmission from person to person may have occurred. Given these events, we are currently in a Pandemic Alert Phase 3, defined by WHO as "human infections with a new subtype but no human-to-human spread or at most rare instances of spread to a close contact."[1]

Pandemic Planning Assumptions

As a result of the widespread emergence and spread of the H5N1 virus among birds, public health experts and government officials are escalating and intensifying their pandemic preparedness planning. Uncertainty about the magnitude of the next pandemic mandates planning for a severe pandemic such as occurred in 1918. Characteristics of an influenza pandemic that must be considered in strategic planning include:

- The ability of the virus to spread rapidly worldwide;
- The fact that people may be asymptomatic while infectious;
- Simultaneous or near-simultaneous outbreaks in communities across the U.S., thereby limiting the ability of any jurisdiction to provide support and assistance to other areas;
- Enormous demands on the healthcare system;
- Delays and shortages in the availability of vaccines and antiviral drugs; and
- Potential disruption of national and community infrastructures including transportation, commerce, utilities and public safety due to widespread illness and death among workers and their families and concern about on-going exposure to the virus.

[1] http://www.who.int/csr/resources/publications/influenza/whocdscsredc991.pdf

Doctrine for HHS Pandemic Influenza Planning and Response

The ongoing outbreaks of avian influenza in Asia and the progression from the interpandemic period (the period prior to human infections) to a pandemic alert (once human infections have occurred) have prompted HHS to enhance its preparedness planning and activities. In addition to the characteristics of a pandemic noted above, HHS' preparedness planning and response activities are guided by the following principles:

1. Preparedness will require coordination among federal, state and local government and partners in the private sector.
2. An informed and responsive public is essential to minimizing the health effects of a pandemic and the resulting consequences to society.
3. Domestic vaccine production capacity sufficient to provide vaccine for the entire U.S. population is critical, as is development of vaccine against each circulating influenza virus with pandemic potential and acquisition of sufficient quantities to help protect first responders and other critical personnel at the onset of a pandemic.
4. Quantities of antiviral drugs sufficient to treat 25% of the U.S. population should be stockpiled.
5. Sustained human-to-human transmission anywhere in the world will be the triggering event to initiate a pandemic response by the United States.
6. When possible and appropriate, protective public health measures will be employed to attempt to reduce person-to-person viral transmission and prevent or delay influenza outbreaks.
7. At the onset of a pandemic, vaccine, which will initially be in short supply, will be procured by HHS and distributed to state and local health departments for immunization of pre-determined priority groups.
8. At the onset of a pandemic, antiviral drugs from public stockpiles will be distributed to health care providers for administration to pre-determined priority groups.

Sustained human-to-human transmission anywhere in the world will be the triggering event to initiate a pandemic response by the United States.

Key Pandemic Response Elements and Capabilities for Effective Implementation

The nature of the HHS response will be guided by the epidemiologic features of the virus and the course of the pandemic. An influenza pandemic will place extraordinary and sustained demands not only on public health and health care providers, but also on providers of essential services across the United States and around the globe. Realizing that pandemic influenza preparedness is a process, not an isolated event, to most effectively implement key pandemic response actions, specific capabilities must be developed through preparedness activities implemented before the pandemic occurs. This plan outlines key actions for an effective pandemic response, involving surveillance, investigation, protective public health measures; vaccines and antiviral drug production; healthcare and emergency response; and communications and public outreach. In addition, the **Strategic Plan** sorts these actions by the WHO Pandemic phases. Recognizing that this potential public health catastrophe can occur at any time, HHS has aggressively embarked on preparing for a pandemic.

Surveillance, Investigation, Protective Public Health Measures

Aggressive surveillance measures ensure early detection and isolation of novel virus strains. Since a new virus could emerge anywhere in the world, surveillance activities must be conducted globally. To date, working with our international partners, HHS has greatly intensified its U.S. and global surveillance activities. In addition, HHS is developing comprehensive infection control strategies.

Once sustained human infection is documented, early in a pandemic, especially before a vaccine is available or during a period of limited supply, HHS may implement travel-related and community-based public health strategies in order to impede the spread of the virus and reduce the number of people infected. In particular, travel advisories and precautions, screening of persons arriving from affected areas, closing schools, restricting public gatherings, quarantine of exposed persons and isolation of infected persons may be implemented with the intent of slowing introduction and transmission of the virus. The use and continuation of these interventions will be determined by assessments of their effectiveness.

Vaccines and Antiviral Drugs

Vaccines and antiviral drugs have the potential to significantly reduce morbidity and mortality during a pandemic. In addition, vaccines and antiviral drugs may also limit viral spread. Although antiviral drugs can be stockpiled, a pandemic vaccine can only be made once the pandemic virus is identified. HHS is currently initiating vaccine development and clinical testing leading toward a vaccine that may provide complete or partial protection against potential pandemic viral strains and also increasing and diversifying antiviral medicines in the Strategic National Stockpile (SNS), a cache of medical and pharmaceutical supplies maintained by HHS. FDA is currently working with industry to facilitate the development, licensure/approval, production and availability of pandemic influenza countermeasures.

At the onset of a pandemic, HHS will accelerate its ongoing work with industry to facilitate the production and distribution of antiviral drugs and pandemic vaccines. HHS will continue to monitor antiviral drug and pandemic vaccine distribution effectiveness, and adverse events Since vaccine and antiviral drugs are likely to be in short supply at the onset of an influenza pandemic, identification of predefined groups in which these medications will be used will be discussed as part of federal planning activities. HHS will work with state and local governments to develop guidelines and operational plans for the distribution of available supplies of a pandemic vaccine and antiviral drugs.

Healthcare and Emergency Response

An effective healthcare and emergency response requires planning and coordination among all levels of government and providers of direct patient care and essential services. HHS is working with its state and local partners to increase health care surge capacity of medical equipment, materials and personnel.

During a pandemic, HHS will work with states and local governments, and the private sector to optimize healthcare and emergency response. Since a pandemic may unfold in an unpredictable way, HHS actions in a pandemic will be shaped by regular assessments and adjustments of its strategies.

Communications and Public Outreach

Dissemination of information to all Americans is a critical component of effective pandemic planning and response. HHS is currently developing communication and outreach materials and messages. In addition, HHS is developing strategies to address psychosocial concerns and procedures for implementation of communications plans for health care providers and the public.

During a pandemic, HHS will provide honest, accurate and timely information on the pandemic to the public. It will also monitor and evaluate its interventions and will communicate lessons learned to healthcare providers and public health agencies on the effectiveness of clinical and public health responses.

All state, local, and tribal governments must be prepared to detect the earliest cases of pandemic influenza infection and disease, to minimize illness and morbidity, and to decrease social disruption and economic loss.

Part 2 – Public Health Guidance to State and Local Partners

All state, local, and tribal governments must be prepared to detect the earliest cases of pandemic influenza infection and disease, to minimize illness and morbidity, and to decrease social disruption and economic loss. Specific guidance and recommendations for pandemic influenza preparedness for state, local and tribal governments are detailed in eleven supplements in Part 2.

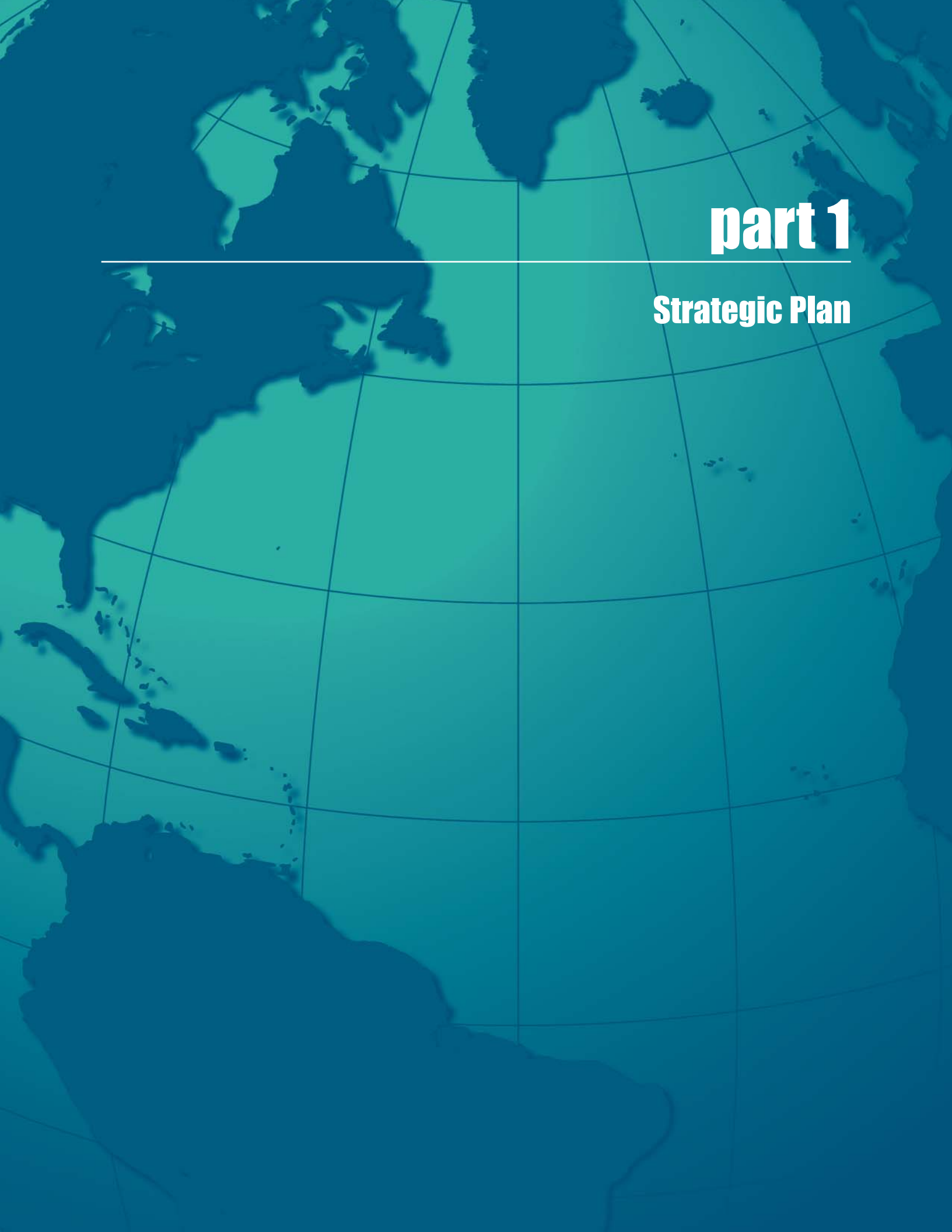
- **Surveillance (Supplement 1)** provides recommendations to state and local partners on surveillance for influenza viruses and disease to monitor the health impact of influenza throughout the pandemic phases.
- **Laboratory Diagnostics (Supplement 2)** provides recommendations to state and local public health partners and other laboratories on the use of diagnostic tests to detect, characterize, and monitor novel subtypes of influenza, including avian influenza A (H5N1) and other viruses with pandemic potential.
- **Healthcare Planning (Supplement 3)** provides healthcare partners with recommendations for developing plans to respond to an influenza pandemic with a focus on planning for pandemic influenza surveillance, decision-making structures for responding to a pandemic, hospital communications, education and training, patient triage, clinical evaluation and admission, facility access, occupational health, distribution of vaccines and antiviral drugs, surge capacity, and mortuary issues. Planning for the provision of care in non-hospital settings—including residential care facilities, physicians' offices, private home healthcare services, emergency medical services, federally qualified health centers, rural health clinics, and alternative care sites—is also addressed.
- **Infection Control (Supplement 4)** provides guidance to healthcare and public health partners on basic principles of infection control for limiting the spread of pandemic influenza including the selection and use of personal protective equipment; hand hygiene and safe work practices; cleaning and disinfection of environmental surfaces; handling of laboratory specimens; and post-mortem care. The guidance also covers infection control practices related to the management of infectious patients, the protection of persons at high-risk for severe influenza or its complications, and issues concerning occupational health.
- **Clinical Guidelines (Supplement 5)** provides clinical procedures for the initial screening, assessment, and management of patients with suspected novel influenza during the Interpandemic and Pandemic Alert Periods and for patients with suspected pandemic influenza during the Pandemic Period.

Robust preparedness for the next pandemic requires coordination with state and local emergency responders.

HHS encourages all levels of government to use this plan and begin refining their own.

- **Vaccine Distribution and Use (Supplement 6)** provides recommendations to state and local partners and other stakeholders on planning for the different elements of a pandemic vaccination program, including vaccine distribution, vaccination of priority groups, monitoring of adverse events, tracking of vaccine supply and administration, vaccine coverage and effectiveness studies, communications, legal preparedness, training, data collection on use, effectiveness, safety and the development of drug resistance.
- **Antiviral Drug Distribution and Use (Supplement 7)** provides recommendations to state and local partners on the distribution and use of antiviral drugs for treatment and prophylaxis throughout the pandemic phases, including issues such as procurement, distribution to pre-defined priority groups, legal preparedness, training and data collection.
- **Community Disease Control and Prevention (Supplement 8)** provides recommendations to state and local partners on the use of disease containment strategies to prevent or decrease transmission during different pandemic phases.
- **Managing Travel-Related Risks of Disease (Supplement 9)** provides recommendations to state and local partners on travel-related containment strategies that can be used during different phases of an influenza pandemic, including strategies that range from distribution of travel health alert notices, to isolation and quarantine of new arrivals, to restriction or cancellation of nonessential travel.
- **Public Health Communications (Supplement 10)** outlines key influenza pandemic risk communications concepts including:
  - When health risks are uncertain, as likely will be the case during an influenza pandemic, people need information about what is known and unknown, as well as interim guidance to formulate decisions to help protect their health and the health of others;
  - An influenza pandemic will generate immediate, intense, and sustained demand for information from the public, healthcare providers, policy makers, and news media;
  - Timely and transparent dissemination of clear, accurate, science-based, culturally competent information about pandemic influenza and the progress of the response can build public trust and confidence;
  - Coordination of message development and release of information among federal, state, and local health officials is critical to help avoid confusion that can undermine public trust, raise fear and anxiety, and impede response measures;
  - Information to public audiences should be technically correct and sufficiently complete to encourage support of policies and official actions.
- **Workforce Support: Psychosocial Considerations and Information Needs (Supplement 11)** focuses on the institutionalization of psychosocial support services that will help workers manage emotional stress during the response to an influenza pandemic and resolve related personal, professional, and family issues.

Robust preparedness for the next pandemic also requires coordination with state and local emergency responders. HHS encourages all levels of government to use this plan and begin refining their own. To this end, HHS plans to engage all stakeholders in an ongoing dialogue to refine and better coordinate preparedness plans.



part 1

Strategic Plan

strategic plan

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the pandemic influenza threat

Influenza A viruses have infected many different animals including ducks, chickens, pigs, whales, horses, and seals. Influenza A viruses normally seen in one species can sometimes cross over and cause illness in another species. This creates the possibility that a new virus will develop, either through mutation or mixing of individual viruses, in turn creating the possibility for new viral strains that can be highly infective, readily transmissible, and highly lethal in humans. When a pandemic virus strain emerges, 25% to 35% of the population could develop clinical disease, and a substantial fraction of these individuals could die. The direct and indirect health costs alone (not including disruptions in trade and other costs to business and industry) have been estimated to approach $181 billion for a moderate pandemic (similar to those in 1957 and 1968) with no interventions. Faced with such a threat, the U.S. and its international partners will need to respond quickly and forcefully to reduce the scope and magnitude of the potentially catastrophic consequences.

Such a threat currently exists in the form of the H5N1 virus, which is spreading widely and rapidly in domestic and migratory fowl across Asia and Europe. As of October 2005, this strain has infected more than 115 humans, killing approximately 50% of those known to be infected. The virus is now endemic in many bird species so that elimination of the virus is not feasible. If this virus mutates in such a way that it becomes capable of spreading efficiently from person to person, the feared pandemic could become a reality. (Additional background information is provided in Appendix B.)

When a pandemic virus strain emerges, 25% to 35% of the population could develop clinical disease, and a substantial fraction of these individuals could die.

Emergence of a human influenza virus with pandemic potential presents a formidable response challenge. If such a strain emerged in one or a few isolated communities abroad or within the U.S. and was detected quickly, containment of the outbreak(s), though very difficult, might be feasible, thereby preventing or significantly retarding the spread of disease to other communities. Containment attempts would require stringent infection-control measures such as bans on large public gatherings, isolation of symptomatic individuals, prophylaxis of the entire community with antiviral drugs, and various forms of movement restrictions—possibly even including a quarantine.

The resources required for such vigorous containment would almost certainly exceed those available in the affected community(ies). Thus, if a containment attempt is to have a chance of succeeding, the response must employ the assets of multiple partners in a well coordinated way. For isolated outbreaks outside the U.S., this means effective multinational cooperation in executing containment protocols designed and exercised well in advance. For isolated outbreaks within the U.S., this would require effective integration of the response assets of local, state, and federal governments and those of the private sector.

The National Response Plan (NRP), based on the principles of incident management, provides an appropriate conceptual and operational framework for a multi-party response to an outbreak of a potential influenza pandemic in one or a few U.S. communities. In particular, the NRP is designed to engage the response assets of multiple public and private partners and bring them to bear in a coordinated way at one or a few incident sites. (Appendix A provides additional information regarding the NRP.)

If efforts to contain isolated outbreaks within the U.S. were unsuccessful and influenza spread quickly to affect many more communities either simultaneously or in quick succession—the hallmark of a pandemic—response assets at all levels of government and the private sector would be taxed severely. Communities would need to direct all their influenza response assets to their own needs and would have little to spare for the needs of others. Moreover, as the number of affected communities grows, their collective need would spread the response assets of states and the federal government ever thinner. In the extreme, until a vaccine against the pandemic virus would become available in sufficient quantity to have a significant impact on protecting public health, thousands of communities could be countering influenza simultaneously with little or no assistance from adjacent communities, the state, or the federal government. Preparedness planning for pandemic influenza response must take this prospect into account.

planning assumptions

Pandemic preparedness planning is based on assumptions regarding the evolution and impacts of a pandemic. Defining the potential magnitude of a pandemic is difficult because of the large differences in severity for the three 20th-century pandemics. While the 1918 pandemic resulted in an estimated 500,000 deaths in the U.S., the 1968 pandemic caused an estimated 34,000 U.S. deaths. This difference is largely related to the severity of infections and the virulence of the influenza viruses that caused the pandemics. The 20th century pandemics have also shared similar characteristics. In each pandemic, about 30% of the U.S. population developed illness, with about half seeking medical care. Children have tended to have the highest rates of illness, though not of severe disease and death. Geographical spread in each pandemic was rapid and virtually all communities experienced outbreaks.

Pandemic planning is based on the following assumptions about pandemic disease:

- Susceptibility to the pandemic influenza subtype will be universal.
- The clinical disease attack rate will be 30% in the overall population. Illness rates will be highest among school-aged children (about 40%) and decline with age. Among working adults, an average of 20% will become ill during a community outbreak.
- Of those who become ill with influenza, 50% will seek outpatient medical care.
- The number of hospitalizations and deaths will depend on the virulence of the pandemic virus. Estimates differ about 10-fold between more and less severe scenarios. Because the virulence of the influenza virus that causes the next pandemic cannot be predicted, two scenarios are presented based on extrapolation of past pandemic experience (Table 1).

Table 1. Number of Episodes of Illness, Healthcare Utilization, and Death Associated with Moderate and Severe Pandemic Influenza Scenarios*

Characteristic	Moderate (1958/68-like)	Severe (1918-like)
Illness	90 million (30%)	90 million (30%)
Outpatient medical care	45 million (50%)	45 million (50%)
Hospitalization	865,000	9,900,000
ICU care	128,750	1,485,000
Mechanical ventilation	64,875	742,500
Deaths	209,000	1,903,000

*Estimates based on extrapolation from past pandemics in the United States. Note that these estimates do not include the potential impact of interventions not available during the 20th century pandemics.

Risk groups for severe and fatal infections cannot be predicted with certainty.

- Risk groups for severe and fatal infections cannot be predicted with certainty. During annual fall and winter influenza season, infants and the elderly, persons with chronic illnesses, and pregnant women are usually at higher risk of complications from influenza infections. In contrast, in the 1918 pandemic, most deaths occurred among young, previously healthy adults.
- The typical incubation period (the time between acquiring the infection until becoming ill), for influenza averages 2 days. We assume this would be the same for a novel strain that is transmitted between people by respiratory secretions.
- Persons who become ill may shed virus and can transmit infection for one-half to one day before the onset of illness. Viral shedding and the risk for transmission will be greatest during the first 2 days of illness. Children will shed the greatest amount of virus and, therefore are likely to pose the greatest risk for transmission.
- On average about 2 secondary infections will occur as a result of transmission from someone who is ill. Some estimates from past pandemics have been higher, with up to about 3 secondary infections per primary case.
- In an affected community, a pandemic outbreak will last about 6 to 8 weeks. At least two pandemic disease waves are likely. Following the pandemic, the new viral subtype is likely to continue circulating and to contribute to seasonal influenza.
- The seasonality of a pandemic cannot be predicted with certainty. The largest waves in the U.S. during 20th century pandemics occurred in the fall and winter. Experience from the 1957 pandemic may be instructive in that the first U.S. cases occurred in June but no community outbreaks occurred until August and the first wave of illness peaked in October.

In an affected community, a pandemic outbreak will last about 6 to 8 weeks.
At least two pandemic disease waves are likely.

doctrine for a pandemic

HHS will be guided by the following principles in initiating and directing its response activities:

1) In advance of an influenza pandemic, HHS will work with federal, state, and local government partners and the private sector to coordinate pandemic influenza preparedness activities and to achieve interoperable response capabilities.[2]
2) In advance of an influenza pandemic, HHS will encourage all Americans to be active partners in preparing their states, local communities, workplaces, and homes for pandemic influenza and will emphasize that a pandemic will require Americans to make difficult choices. An informed and responsive public is essential to minimizing the health effects of a pandemic and the resulting consequences to society.
3) In advance of an influenza pandemic, HHS, in concert with federal partners, will work with the pharmaceutical industry to develop domestic vaccine production capacity sufficient to provide vaccine for the entire U.S. population as soon as possible after the onset of a pandemic and, during the pre-pandemic period, to produce up to 20 million courses of vaccine against each circulating influenza virus with pandemic potential and to expand seasonal influenza domestic vaccine production to cover all Americans for whom vaccine is recommended through normal commercial transactions.
4) In advance of an influenza pandemic, HHS, in concert with federal partners and in collaboration with the States, will procure sufficient quantities of antiviral drugs to treat 25% of the U.S. population and, in so doing, stimulate development of expanded domestic production capacity sufficient to accommodate subsequent needs through normal commercial transactions. HHS will stockpile antiviral medications in the Strategic National Stockpile, and states will create and maintain local stockpiles.
5) Sustained human-to-human transmission anywhere in the world will be the triggering event to initiate a pandemic response by the United States. Because we live in a global community, a human outbreak anywhere means risk everywhere.
6) The US will attempt to prevent an influenza pandemic or delay its emergence by striving to arrest isolated outbreaks of a novel influenza wherever circumstances suggest that such an attempt might be successful, acting in concert with WHO and other nations as appropriate. At the core of this strategy will be basic public health measures to reduce person-to-person transmission.

[2] Throughout this document, the term "state and local" is inclusive of municipal, county, territorial, and tribal governments and health authorities.

In advance of an influenza pandemic, HHS will encourage all Americans to be active partners in preparing their states, local communities, workplaces, and homes for pandemic influenza and will emphasize that a pandemic will require Americans to make difficult choices.

7) At the onset of an influenza pandemic, HHS, in concert with federal partners, will work with the pharmaceutical industry to procure vaccine directed against the pandemic strain and to distribute vaccine to state and local public health departments for pre-determined priority groups based on pre-approved state plans.

8) At the onset of an influenza pandemic, HHS, in collaboration with the states, will begin to distribute and deliver antiviral drugs from public stockpiles to healthcare facilities and others with direct patient care responsibility for administration to pre-determined priority groups.

key pandemic influenza response

An influenza pandemic will place extraordinary and sustained demands on public health and healthcare systems and on providers of essential community services across the U.S. and throughout the world. The nature and scope of these demands will vary over the course of the pandemic. Table 2 lists key pandemic response actions that public health, medical, and other government authorities at all levels must be prepared to take to mitigate the potentially catastrophic consequences of a pandemic. A more detailed list of HHS-specific response actions categorized by WHO pandemic phase is shown in Tables 4 through 9.

Pandemic influenza preparedness is a process, not an isolated event. To most effectively implement key pandemic response actions, specific capabilities must be developed through preparedness activities implemented before the pandemic occurs. For each key pandemic response activity, Table 2 summarizes capabilities needed for implementation of an effective response.

An influenza pandemic will place extraordinary and sustained demands on public health and healthcare systems and on providers of essential community services across the U.S. and throughout the world.

Table 2. Key Pandemic Response Elements and Key Capabilities for their Effective Implementation

Key Pandemic Response Actions	Key Capabilities Needed for Implementation of an Effective Response
Surveillance, Investigation, and Protective Public Health Measures	
1. Increase international surveillance and collaborate in outbreak investigation to track the emerging epidemiological patterns and impacts of disease caused by the novel influenza virus subtype.	**1.** Agreements with international partners, including international organizations, and other U.S. government agencies, to improve the capability and capacity of local public health systems in countries where a potential pandemic virus strain is likely to emerge so that accurate and timely influenza surveillance information can be obtained.
2. Determine feasibility of containing the initial outbreak of a potential pandemic, working in consultation with international partners, and if feasible, implement containment activities.	**2.** Assets (people, facilities, equipment, supplies, and exercised procedures), deployed at home and abroad, to investigate, and if feasible, mount an immediate emergency response.
3. Obtain samples of the potential pandemic virus from infected people and distribute them to laboratories for genetic, antigenic, and antiviral resistance analysis. Prepare reference strains for distribution to vaccine manufacturers. Assess cross-protection of stockpiled vaccine, if available, against the pandemic virus.	**3.** Laboratory assets to characterize the novel influenza virus strain (genetic and antigenic characteristics and antiviral resistance) and rapidly develop a vaccine reference strain for distribution to manufacturers. Agreements with international partners to quickly obtain samples.
4. Implement surveillance and control measures (e.g., isolation of cases, quarantine of contacts, antiviral drug treatment and prophylaxis) at points-of-entry to decrease introduction and spread of the pandemic virus in the U.S.	**4.** Quarantine stations and related protections at all major U.S. ports of entry to limit the introduction of pandemic influenza, isolate cases, and trace contacts.
5. Enhance domestic surveillance to detect pandemic outbreaks, track the spread of virus in near real-time, and assess impacts on health and infrastructure.	**5.** Real-time or near real-time electronic connectivity with major domestic healthcare institutions and public health departments across the U.S. to obtain daily influenza disease and resource availability information. Widely available, reliable, rapid, sensitive, and accurate diagnostic tests.
6. Implement public health measures to limit the spread of infection (e.g., canceling public gatherings) as well as individual measures to decrease the risk of acquiring or spreading infection (e.g., personal hygiene, isolation of ill persons).	**6.** Assets (people, facilities, equipment, supplies, and exercised procedures) to effect wide-spread individual and community-based infection control measures and educate individuals on personal protection strategies.
7. Monitor pandemic response actions and assess their effectiveness.	**7.** Assets (people, facilities, equipment, supplies, and exercised procedures) to analyze data continually during the course of the pandemic to guide response activities and to assess the safety and efficacy of interventions.

Table 2. (Continued)

Key Pandemic Response Actions	Key Capabilities Needed for Implementation of an Effective Response
Vaccines and Antiviral Drugs	
1. Consider administration of pre-pandemic stockpiled vaccine, if available, to pre-defined groups critical to the pandemic response. This could provide partial immune protection and/or prime the immune system for a protective response once a targeted pandemic vaccine becomes available.	**1.** A national stockpile of 40 million doses (2 doses per person) of vaccine against influenza virus subtypes considered to pose a substantial pandemic risk (currently avian H5N1).
2. In conjunction with other parties, manufacture, test, license, and produce vaccine against the specific pandemic virus strain.	**2.** Domestic influenza vaccine manufacturing capacity to produce sufficient pandemic vaccine for the U.S. population within 6 months of the onset of an influenza pandemic. Consider liability concerns vaccine manufacturers. A library of reference strains and reagents for novel influenza subtypes; clinical trials of candidate pandemic influenza vaccines in the U.S. and affected areas.
3. Allocate and administer pandemic vaccine to pre-defined priority groups. Ensure security for protection of scarce vaccines.	**3.** State and local vaccine distribution plans, guided by recommendations for use of pandemic vaccine when supply is short, that are specific, implementable, and which have been practiced in tabletop and field exercises.
4. Monitor vaccine coverage and track vaccine use so persons who receive initial pandemic vaccine can return for a second dose, if required. Monitor for adverse events following vaccination and conduct studies to assess vaccine safety and effectiveness.	**4.** Assets (people, facilities, equipment, supplies, and exercised procedures) to monitor vaccine coverage, adverse events, and effectiveness.
5. Allocate stockpiled antiviral drugs for use in pre-defined high-risk and critical infrastructure populations.	**5.** Availability of at least 81 million treatment courses of approved antiviral drugs—enough for treatment of approximately 25% of the U.S. population and 6 million additional treatment courses in reserve for domestic containment. State and local antiviral drug distribution plans, guided by recommendations for use of pandemic vaccine when supply is short, that are specific, implementable, and have been practiced in tabletop and field exercises. Increased U.S.-based antiviral drug manufacturing.

Table 2. (Continued)

Key Pandemic Response Actions	Key Capabilities Needed for Implementation of an Effective Response
Vaccines and Antiviral Drugs (Continued)	
6. Monitor antiviral drug distribution and adverse events, and conduct studies to further assess safety and effectiveness.	**6.** Assets (people, facilities, equipment, supplies, and exercised procedures) to monitor antiviral distribution, adverse events, and effectiveness.
Healthcare and Emergency Response	
1. Distribute stockpiled ventilators and other medical material needed to treat and care for infected individuals to health departments and federal agencies that provide direct patient care.	**1.** Equipment and supplies maintained in the Strategic National Stockpile and state stockpiles sufficient to enhance medical surge capacity.
2. Deploy Federal Medical Stations, as available, to provide healthcare surge capacity in hardest hit areas.	**2.** Federal Medical Stations and healthcare assets (people, facilities, equipment, supplies, and exercised procedures) to enhance medical surge capacity.
3. Test patient specimens using highly accurate (sensitive and specific) rapid diagnostic tests to identify pandemic outbreaks in communities and contribute to management decisions.	**3.** Widely available accurate rapid diagnostic methods to detect and characterize influenza viruses.
4. Assist communities with surge mortuary services to accommodate a large number of expected fatalities.	**4.** Assets (people, facilities, equipment, supplies, and exercised procedures) for the timely, safe, and respectful disposition of the deceased.
5. Provide psychosocial support to responders and affected communities.	**5.** Institutionalization of psychosocial support services and development of workforce resiliency programs.
Communications and Outreach	
1. Public education and information campaign to 1) communicate measures the public can implement to minimize risk and decrease the spread of infection; 2) provide honest, accurate, understandable and timely information; and 3) counter confusion and panic.	**1.** Pre-tested risk communication materials that provide the public easy-to-understand information regarding pandemic influenza and how individuals can protect themselves and help others during an influenza pandemic, and appropriate use of vaccines and antiviral drugs. Pre-tested procedures through which public authorities within each community will provide information and guidance to the public (including marginalized, disadvantaged, and foreign-language populations) during an influenza pandemic.

roles and responsibilities of HHS agencies and offices

Table 3 provides a summary of the roles and responsibilities assigned to select HHS officials, agencies, and divisions.

Table 3. Summary of Major Pandemic Response Roles of HHS Officials, Agencies, and Divisions

HHS Official, Agency, or Division	Roles
Secretary of Health and Human Services	■ Directs all HHS pandemic response activities
Assistant Secretary for Public Health Emergency Preparedness (ASPHEP)	■ Coordinates HHS pandemic response activities ■ Monitors effectiveness of response activities and modifies strategies, as needed ■ Coordinates and communicates with other federal departments and agencies
Assistant Secretary for Health (ASH)	■ Directs the Office of the Surgeon General in deployment of U.S. Public Health Service Commissioned Corps assets ■ Directs Regional Health Administrators who will be members of Secretary's Emergency Response Teams (SERTs) in their regions ■ Advises Secretary on Public Health and Science as he directs HHS pandemic response activities ■ Coordinates operations planning efforts of HHS agencies, operational divisions and offices ■ Assists with public communications and coordination with state and local public health partners ■ Directs the National Vaccine Program Office (NVPO) in pandemic preparedness and response
Director of Office of Intergovernmental Affairs	■ Advises and coordinates outreach and communications to state, local and tribal officials and national intergovernmental organizations
Assistant Secretary for Legislation (ASL)	■ Coordinates Congressional outreach and communications
Office of the Surgeon General (OSG)	■ Deploys U.S. Public Health Service Commissioned Corps assets (upon approval of the Assistant Secretary for Health) ■ Assists with public communication and education ■ Assists and coordinate pandemic planning with partner federal health service providers, specifically the Indian Health Service, The Federal Bureau of Prisons and the Coast Guard
Assistant Secretary for Public Affairs (ASPA)	■ Coordinates public information and communications
National Vaccine Program Office (NVPO)	■ Chairs Secretary's Task Force on Influenza Preparedness ■ Coordinates communication between vaccine and antiviral drug manufacturers and HHS agencies ■ Coordinates development of after-action report and lessons learned ■ Maintains close communication with drug and vaccine manufacturers

Table 3. (Continued)

HHS Official, Agency, or Division	Roles
Office of the General Counsel (OGC)	■ Advises on legal issues and authorities related to key pandemic response activities
Director of the Office of Global Health Affairs (OGHA)	■ Coordinates interactions with health authorities in other governments and international organizations in coordination with the Department of State
Centers for Disease Control and Prevention (CDC)	■ Conducts and supports clinical and virological influenza surveillance ■ Monitors pandemic health impacts ■ Implements travel-related and community containment measures as necessary to prevent the introduction, transmission, and spread of pandemic disease from foreign countries into the US, from state to state or in the event of inadequate local control ■ Coordinates pandemic response activities with state, local and tribal public health agencies ■ Investigates epidemiology and clinical characteristics of pandemic disease ■ Assists in vaccination program implementation and in monitoring and investigating vaccine adverse events ■ Assesses vaccine effectiveness in population-based studies ■ Coordinates antiviral and other drug delivery from the Strategic National Stockpile ■ Monitors antiviral drug use, effectiveness, safety, and resistance ■ Monitors the implementation/effectiveness of protective public health measures ■ Recommends and evaluates community measures to prevent and control disease ■ Makes recommendations on diagnosis and management of influenza illness ■ Makes recommendations on appropriate infection control recommendations ■ Communicates with state and local health departments and other public health partners ■ Communicates information on pandemic health impacts as directed by the ASPA ■ Maintains close communication with drug and vaccine manufacturers
Centers for Medicare and Medicaid	■ Provides streamlined payment mechanisms and works with prescription drug plans and Medicare managed care plans, as necessary to ensure ready access to pandemic influenza vaccine and antiviral prescription drugs for Medicare's population ■ Communicates specific guidance and supports pandemic flu response activities of the nation's hospitals, home health agencies, skilled nursing facilities and other health care providers, suppliers and practitioners that participate in Medicare and Medicaid

Table 3. (Continued)

HHS Official, Agency, or Division	Roles
	■ Communicates influenza pandemic related information through existing outreach networks to Medicare beneficiary populations ■ Supports tracking and surveillance of Medicare patients, including high-risk and vulnerable patients who have received pandemic influenza vaccine and antiviral prescription drugs, including review of Medicare claims and quality data ■ Supplies "real time" intelligence to other Federal health care agencies on the status of local, regional and national pandemic flu response provider activities through stakeholder association meetings and open door forums ■ Prepares reference strains appropriate for vaccine manufacturing
Food and Drug Administration (FDA)	■ Regulates manufacturing process ■ Evaluates and licenses pandemic vaccines ■ Evaluates and approves antiviral drugs for influenza ■ Facilitates the development, evaluation and clearance or approval of diagnostic tests and devices ■ Prepares reagents to standardize potency of inactivated influenza vaccines ■ Prepares reference strains appropriate for vaccine manufacturing ■ Reviews antiviral drug and pandemic vaccine supply issues ■ Evaluates and issues Emergency Use Authorizations when appropriate ■ Monitors vaccine adverse events ■ Monitors antiviral drug adverse events ■ Maintains close communication with drug and vaccine manufacturers ■ Evaluates investigational new drug applications (INDs) and investigational device exemptions (IDEs) for medical products that diagnose, treat, prevent or mitigate influenza ■ Evaluates new manufacturing sites and processes for antiviral drugs ■ Makes necessary changes in prescribing and patient information, including dosing, target populations, and other direction for use, for antiviral drugs and pandemic vaccines based on research and adverse events ■ Evaluates long-term stability of stockpiled antiviral drugs for purposes of shelf life extension ■ Monitors to protect against the distribution of counterfeit antiviral drugs and pandemic vaccines

Table 3. (Continued)

HHS Official, Agency, or Division	Roles
National Institutes of Health (NIH)	■ Develops improved drugs against influenza ■ Supports basic research, including structure/function studies of influenza virus proteins with the goal of identifying new therapeutic targets ■ Develops and clinically evaluates novel influenza vaccines and vaccination strategies (e.g., adjuvants, delivery systems) ■ Develops sensitive, specific, and rapid diagnostic tests for influenza ■ Evaluates the immune response to infection and vaccination ■ Determines the molecular basis of virulence in humans and animals ■ Evaluates the molecular and/or environmental factors that influence the transmission of influenza viruses, including drug-resistant strains ■ Studies the evolution and emergence of influenza viruses including the identification of factors that affect influenza host-range and virulence ■ Supports virologic and serologic surveillance studies of the distribution of influenza viruses with pandemic potential in animals ■ Maintains close communication with drug and vaccine manufacturers ■ Prepares reference strains appropriate for vaccine manufacturing
Agency for Healthcare Research and Quality (AHRQ)	■ Communicates with and supports federal, state, and local public health partners on mass vaccination and surge capacity healthcare delivery plans
Health Resources and Services Administration (HRSA)	■ Communicates with and provides technical assistance to support pandemic response activities of state primary care associations, health centers, and other community-based providers ■ Promotes coordination with the National Hospital Bioterrorism Preparedness Program for surge capacity plans
Substance Abuse and Mental Health Services Administration (SAMHSA)	■ Communicates with and supports pandemic response activities of state, local, and tribal mental health and substance abuse agencies ■ Communicates information on behavioral health issues, including stress and anxiety as a result of pandemic health impacts, as directed by the ASPA
Administration for Children and Families (ACF)	■ Communicates with and supports pandemic response activities of state, local, tribal, and nonprofit (including faith-based and community) human services organizations ■ Communicates information on child and family well-being, including the importance and availability of vaccinations and antiviral drugs, as well as proper hygienic practices, to treat pandemic influenza and prevent its spread

Table 3. (Continued)

HHS Official, Agency, or Division	Roles
	■ Encourages the participation of human services providers (e.g., Head Start centers, child care centers, family resource centers, community action agencies, runaway and homeless youth shelters, and shelters for unaccompanied alien children) in making vaccines and antiviral drugs available to vulnerable populations ■ Assists in medium- and long-term social adjustment of individuals, families, and communities following the pandemic
Indian Health Service (IHS)	■ Communicates with and supports state, local, and tribal pandemic response activities at HHS, tribal, and urban Indian sites serving American Indian and Alaska Native populations

HHS actions for pandemic influenza preparedness and response

HHS will follow the WHO published guidance for national pandemic planning, which defines pandemic activities in six phases. WHO Phases 1 and 2 are the Interpandemic Period, which includes phases where no new influenza virus subtypes have been detected in humans.

The Pandemic Alert Period includes a phase when human infection with a novel influenza strain has been identified but no evidence has been found of transmission between people or at most rare instances of spread to a close contact (WHO Phase 3) and includes phases where person-to-person transmission is occurring in clusters with limited human-to-human transmission (WHO Phases 4 and 5). WHO Phase 6 is the Pandemic Period, in which there is increased and sustained transmission in the general population. (Appendix C describes the WHO pandemic phases in detail.)

Each pandemic phase is associated with a range of preparedness and response activities directed by the Secretary of Health and Human Services, after consultation with international authorities and others, as necessary. Given that an influenza pandemic may not unfold in a completely predictable way, decision-makers must regularly reassess their strategies and actions and make adjustments as necessary. This section highlights critical pandemic preparedness and response activities to be implemented by HHS.

Given that an influenza pandemic may not unfold in a completely predictable way, decision-makers must regularly reassess their strategies and actions and make adjustments as necessary.

Table 4: WHO Pandemic Phases 1 and 2: HHS Actions

WHO Phases 1 and 2: Interpandemic Phase Actions	
Planning and Coordination	■ Assess preparedness status and identify actions needed to fill gaps. ■ Coordinate with Federal, state and local, tribal, and private-sector authorities and organizations, and with media and the public. ■ Develop and conduct tabletop and field exercises to evaluate and improve preparedness plans and response capabilities. ■ Coordinate completion of pandemic preparedness and response plans at Federal, state local, tribal, and private-sector levels. ■ Update HHS Pandemic Influenza Plan as needed. ■ Consider indemnification and liability protection issues for affected entities, including pandemic vaccine manufacturers, pandemic vaccine distributors, and healthcare providers who administer pandemic vaccines.
Surveillance, Investigation, and Protective Public Health Measures	■ Prepare reagents for identification of new influenza strains in animals and other strains with pandemic potential. ■ Assist in domestic and international influenza outbreak investigations. ■ Develop strategies to enhance domestic surveillance and collaborate with international organizations to improve global surveillance to allow earlier detection of novel influenza viruses. ■ Enhance collaborations with international organizations and governments to facilitate surveillance and reporting and the ability to investigate disease outbreaks and implement containment measures that could prevent a pandemic. ■ Develop guidance for outbreak control measures in healthcare settings and other institutions such as long-term care facilities. ■ Develop strategies to prevent spread of infection to or within the U.S. from affected areas (e.g., travel advisories or precautions, assessment of travelers returning from affected areas). ■ Assess pathogenicity, antiviral susceptibility, and other characteristics of novel influenza strains.
Vaccines and Antiviral Drugs	■ Develop strategies to increase uptake of annual influenza vaccine. ■ Expand U.S.-based influenza vaccine manufacturing capacity, diversifying vaccine production methods and suppliers. ■ Ensure capacity exists to produce adequate doses of influenza vaccine year-round. ■ Support development, evaluation, and U.S.-based production of an influenza vaccine produced in cell culture. ■ Support development, evaluation and U.S.-based production of antiviral drugs. ■ Develop vaccine reference strain and reagents for influenza strains with pandemic potential.

Table 4. (Continued)

WHO Phases 1 and 2: Interpandemic Phase Actions	
	■ Obtain investigational lots of candidate vaccine for novel influenza strains and conduct clinical testing. ■ Develop strategies for rapid administration of vaccines to priority populations and mechanisms to monitor vaccine effectiveness and safety. ■ Support efforts to make antiviral drugs available to treat priority populations and to support containment, outbreak response, and protection of priority populations involved in pandemic response activities and maintenance of critical services and infrastructures.
Healthcare and Emergency Response	■ Assess surge capacity of medical (including inpatient, outpatient, and long-term care facilities) and emergency response systems (e.g. beds, ventilators, etc.) to meet expected needs during a pandemic. ■ Assess surge capacity of federal medical assets (e.g. IHS, VA, DOD).
Communications and Outreach	■ Coordinate communication activities across federal departments and with state, local and international partners. ■ Inform and educate the public about influenza. ■ Communicate with state and local health departments. ■ Develop educational materials for healthcare and human services providers, the media, and the public on pandemic influenza preparedness and response, including facilities, vaccine, and antiviral drugs in short supply. ■ Develop strategies and materials to support a pandemic response and to promote public trust and decrease fear and anxiety.
Research	■ Conduct research to develop and manufacture new influenza vaccines and antiviral drugs. ■ Conduct research to decrease time needed to develop, evaluate, and produce pandemic vaccine. ■ Conduct research to decrease time needed to develop, evaluate, and produce antiviral drugs. ■ Conduct research on effective protective health measures.

Table 5: WHO Pandemic Phase 3: HHS Actions

WHO Phase 3: Pandemic Alert Phase Actions (No person-to-person transmission)	
Planning and Coordination	■ Assess preparedness status and identify actions needed to fill gaps. ■ Collaborate with international partners to respond to pandemic alert. ■ Inform government officials (including Congress and state health departments) and legislators of pandemic alert status.
Surveillance, Investigation, and Protective Public Health Measures	■ Distribute reagents to state public health laboratories and WHO National Influenza Centers for detection of the new strain. ■ Assist in international influenza outbreak investigations and characterize disease epidemiology and antigenic and genetic characteristics of the virus. ■ Implement strategies to enhance domestic surveillance and to identify suspect cases in the U.S. in coordination with state and local health authorities. ■ Provide guidance to implement outbreak control measures in healthcare settings and other institutions, such as long-term care facilities, as needed. ■ Implement strategies to prevent the spread of infection to or within the U.S. from affected areas, in coordination with state and local health authorities.
Vaccines and Antiviral Drugs	■ Develop vaccine reference strain to the novel influenza virus and distribute to manufacturers. ■ Develop reagents for evaluation of candidate vaccines to the novel strain. ■ Test investigational lots of vaccine to the new strain. ■ Develop a tracking system that will ensure that individuals obtain subsequent doses of vaccine and will report and monitor for adverse events. ■ Develop a tracking system to report and monitor for adverse events in individuals given antiviral therapies. ■ Assess status of available antiviral drugs and strategies for use. ■ Evaluate antiviral susceptibilities of the novel strain.
Healthcare and Emergency Response	■ Assess capacity of medical and emergency response systems to meet expected needs during a pandemic. ■ Enhance surge capacity of federal medical systems.
Communications and Outreach	■ Update state and local health departments, other stakeholders, and the media on status of pandemic. ■ Enhance healthcare provider awareness of the potential for a pandemic and the importance of diagnosis and viral identification for persons with influenza-like illness, especially from potentially affected areas. ■ Implement strategies and disseminate materials to support a pandemic response and to promote public trust and decrease fear and anxiety.

Table 6: WHO Pandemic Phases 4 and 5: HHS Actions

WHO Phases 4 and 5: Pandemic Alert Phase Actions – Limited human-to-human transmission	
Planning and Coordination	■ Assess preparedness status and identify immediate actions needed to fill gaps. ■ Establish coordination of response activities through the Secretary's Operations Center. ■ Coordinate with the WHO and foreign governments. ■ Notify government officials (including Congress and state health departments) and legislators of pandemic status.
Surveillance, Investigation, and Protective Public Health Measures	■ Assist in international containment efforts, if appropriate. ■ Assist in international influenza outbreak investigations and characterize disease epidemiology and antigenic and genetic characteristics of the virus. ■ Distribute reagents to state public health laboratories for detection of the novel strain. ■ Continue enhanced national surveillance; identify suspect cases and/or introduction of a novel virus into the U.S. ■ Provide education to travelers, including refugees being resettled in the U.S., and issue travel advisories, precautions, or restrictions if warranted by disease epidemiology; investigate illness among travelers returning from affected areas and implement isolation and quarantine, as needed.
Vaccines and Antiviral drugs	■ Develop vaccine reference strain (if not already done) and distribute to manufacturers. ■ Develop and test investigational lots of vaccine to the new strain. ■ Develop reagents for formulation and potency testing of pandemic vaccine. ■ Contract with manufacturers to develop pilot lots of pandemic vaccine for clinical testing. ■ Initiate rapid clinical studies of pandemic vaccine safety, immunogenicity, and schedule. ■ Determine susceptibility of the novel influenza strain to antiviral drugs (if not already done). ■ Assess supply, distribution, and production capacity of antiviral drug manufacturers. ■ Contract with manufacturers for production of additional antiviral drugs. ■ Ready process for investigational new drug (IND) or Emergency Use Authorization (EUA) applications for experimental vaccines and antiviral drugs available for use under EUA or IND.

Table 6. (Continued)

WHO Phases 4 and 5: Pandemic Alert Phase Actions – Limited human-to-human transmission	
Healthcare and Emergency Response	■ Assess capacity of medical and emergency response systems to meet expected needs during a pandemic. ■ Provide updated guidance, if indicated, to healthcare providers on clinical management and infection control.
Communications and Outreach	■ Update Congress; state, local, and tribal health departments; local officials, other stakeholders, and the media. ■ Implement public education on the potential for a pandemic and the actions to be taken to reduce risk.

Table 7: WHO Pandemic Phase 6, No U.S. Cases: HHS Actions

WHO Phase 6: Pandemic Period Actions (no cases in the U.S.)	
Planning and Coordination	■ Update government officials (including Congress and state health departments) and legislators on pandemic status. ■ Coordinate information sharing with other federal agencies, including DHS, Department of State, DOD, the WHO, and other countries.
Surveillance, Investigation, and Protective Public Health Measures	■ Collaborate with international organizations to assess epidemiology of disease outbreaks and efficiency of person-to-person transmission, and to obtain parameter estimates to support real-time mathematical modeling. ■ Implement travel advisories, precautions, or restrictions, as appropriate. ■ Investigate illness among travelers returning from affected areas; implement isolation and quarantine, as needed. ■ Assist states, as needed, in investigating potential cases of pandemic influenza. ■ Continue activities to enhance detection of U.S.cases of influenza at borders, hospitals, and outpatient settings. ■ Ensure availability of diagnostic reagents for pandemic influenza strain at state and local public health laboratories. ■ Provide reference laboratory support to test clinical specimens for influenza and identify novel strain. ■ Develop and evaluate diagnostic tests for the novel strain.

Table 7. (Continued)

WHO Phase 6: Pandemic Period Actions (no cases in the U.S.)	
Vaccines and Antiviral drugs	■ Contract with manufacturers for production of pandemic vaccine. ■ Assess candidate vaccines for licensure. ■ Review and revise, as needed, priority groups and strategies for antiviral drug use and vaccination. ■ Continue ongoing assessment of antiviral resistance of the pandemic strain.
Healthcare and Emergency Response	■ Review and revise, as needed, plans for healthcare delivery and community support. ■ Assess availability of federal personnel, supplies, and materials for infection control and clinical care of infected patients. ■ Provide guidance to healthcare providers on infection control guidelines for hospitals, long-term care facilities, and outpatient settings.
Communications and Outreach	■ Update stakeholders and the media through regular briefings. ■ Educate healthcare providers through satellite broadcasts, webcasts, and other communications channels. ■ Continue public education activities.

Table 8: WHO Pandemic Phase 6, U.S. Cases: HHS Actions

WHO Phase 6: Pandemic Period Actions (cases in the U.S.)	
Planning and Coordination	■ Make determination of pandemic disease in the U.S. ■ Assess need for funding for costs associated with pandemic response. ■ Coordinate with international organizations and foreign governments as well as state and local governments.
Surveillance, Investigation, and Protective Public Health Measures	■ Investigate initial cases and outbreaks; consider/implement interventions to decrease disease spread. ■ Implement studies of spread in communities and families; identify risk factors for infection and adverse health outcomes. ■ Reassess containment strategies such as travel advisories and restrictions. ■ Provide laboratory support to health departments in affected areas. ■ Initiate active reporting of enhanced surveillance for mortality and severe morbidity in affected areas. ■ Assist state and local health agencies in responding to outbreaks.

Table 8. (Continued)

WHO Phase 6: Pandemic Period Actions (cases in the U.S.)	
	■ Consult with state and local public health agencies on implementation of strategies to control disease spread and decrease infection rates in communities, as needed. ■ Assess impacts of community control strategies. ■ Assess the effectiveness of public health measures and outbreak control.
Vaccines and Antiviral drugs	■ Review/revise priority populations for vaccination and antiviral drug use. ■ Negotiate production and purchase of pandemic vaccine from manufacturers. ■ Begin distribution of pandemic vaccine, if available, and immunization of target groups. ■ Assist in providing resources and personnel for vaccine administration. ■ Monitor vaccine coverage and vaccine adverse events. ■ Conduct studies of vaccine effectiveness; re-evaluate vaccine dose and schedule. ■ Implement distribution of the antiviral stockpile. ■ Monitor antiviral drug distribution and adverse events. ■ Conduct studies of antiviral drug impacts. ■ Review and approve, as appropriate, IND or EUA applications.
Healthcare and Emergency Response	■ Advise states and localities to activate plans to coordinate healthcare delivery and community response. ■ Deploy medical personnel, equipment, and supplies to augment local healthcare capacity in affected areas. ■ Evaluate clinical outcomes and define optimal treatment strategies.
Communications and Outreach	■ Activate pandemic communications plan. ■ Reinforce education on care seeking and home care. ■ Communicate lessons learned to healthcare providers and public health agencies on effectiveness of clinical and public health responses.
Research	■ Evaluate effectiveness of vaccine, antiviral drugs, and other interventions.

Table 9: WHO Pandemic Phase 6, Between Pandemic Waves or Pandemic Subsided in the U.S: HHS Actions

WHO Phase 6: Pandemic Period Actions (between pandemic waves or pandemic subsided in the U.S.)	
Planning and Coordination	■ Assess coordination during period of pandemic disease and revise response plans, as needed. ■ Implement after-action review of pandemic response activities. ■ Assess resources and authorities that may be needed for subsequent pandemic waves.
Surveillance, Investigation, and Protective Public Health Measures	■ Estimate overall pandemic health impacts including mortality and severe morbidity. ■ Continue enhanced domestic and international surveillance to detect further pandemic waves.
Vaccines and Antiviral drugs	■ Assess vaccine coverage, effectiveness of targeting to priority groups, and efficiency of distribution and administration; determine number of persons who remain unprotected. ■ Assess vaccine efficacy, safety, and impact during the pandemic. ■ Determine potential vaccine formulation changes to improve efficacy or supply. ■ Monitor continued administration of vaccine to persons not previously protected. ■ Assess antiviral effectiveness and safety. ■ Evaluate need to expand vaccine and antiviral production capacity.
Healthcare and Emergency Response	■ Assess effectiveness of federal healthcare and service delivery during prior pandemic phases and revise plans, as needed.
Communications and Outreach	■ Assess effectiveness of communications during prior pandemic phases and revise plans, as needed. ■ Communicate with healthcare providers, the media, and the public about the likely next pandemic wave.
Research	■ Evaluate effectiveness of vaccine, antiviral drugs, and other interventions.

appendices

appendices

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appendix A: national response plan

An influenza pandemic may require activation of the National Response Plan (NRP), especially if the first appearance of the disease in the United States occurs in one or a few isolated communities and an intense multi-party containment effort led by the federal government seems feasible. The Department of Homeland Security (DHS), in collaboration with HHS and other response partners, developed the NRP and the associated National Incident Management System (NIMS) pursuant to the requirements of Homeland Security Presidential Directive (HSPD) #5 – Management of Domestic Incidents. Full descriptions of the NRP and the NIMS, respectively, are available at www.dhs.gov/interweb/assetlibrary/NRP_FullText.pdf and www.fema.gov/nims/nims_compliance.shtm#nimsdocument.

The intent of the NRP is to reduce America's vulnerability to terrorism, major disasters, and other emergencies; to minimize the damage resulting from these emergencies; and to facilitate recovery. The NIMS aligns the special-purpose incident management and emergency response plans of federal government agencies into a unitary structure. Together, the NRP and the NIMS provide a conceptual and operational framework to integrate the capabilities and resources of various governmental jurisdictions, incident management and emergency response disciplines, nongovernmental organizations (NGOs), and the private sector into a cohesive, coordinated, and seamless national framework for domestic incident management. The federal government can invoke the NRP partially or fully in the context of a threat, anticipation of a significant event, or the response to a significant event.

Emergency support functions

The NRP applies a functional approach that groups the capabilities of federal government departments and agencies and the American Red Cross into Emergency Support Functions (ESFs) to provide the planning, support, resources, program implementation, and emergency services that are most likely to be needed. The HHS has primary responsibility for implementing ESF #8 - Public Health and Medical Services, which provides the mechanism for coordinated federal government assistance to supplement state, local, and tribal resources in response to public health and medical care needs (to include veterinary and/or animal issues when appropriate) in the face of a potential or actual large-scale public health and medical emergency.

The intent of the NRP is to reduce America's vulnerability to terrorism, major disasters, and other emergencies; to minimize the damage resulting from these emergencies; and to facilitate recovery.

The full set of Emergency Support Functions is as follows:

ESF1	Transportation
ESF2	Communications
ESF3	Public Works and Engineering
ESF4	Firefighting
ESF5	Emergency Management
ESF6	Mass Care, Housing, Human Services
ESF7	Resource Support
ESF8	**Public Health and Medical Services**
ESF9	Urban Search and Rescue
ESF10	Oil and Hazardous Materials Response
ESF11	Agriculture and Natural Resources
ESF12	Energy
ESF13	Public Safety and Security
ESF14	Long-Term Community Recovery and Mitigation
ESF15	External Affairs

ESF #8 provides for supplemental assistance to state, local, and tribal governments in identifying and meeting the public health and medical needs in core functional areas that include assessment of public health and medical needs (including behavioral health); public health surveillance; medical care personnel; fatality management; and medical equipment and supplies. Management of response activities under ESF #8 occurs through the National Response Coordination Center (NRCC), the Interagency Incident Management Group (IIMG), and the Joint Information Center (JIC). Medical response assets internal to HHS (e.g., the U.S. Public Health Service Commissioned Corps) and through ESF #8 supporting organizations (e.g., the Department of Homeland Security's National Disaster Medical System [NDMS]) may be deployed along with assets from the Strategic National Stockpile (SNS). A complete description of ESF #8 actions and authorities is included in the Public Health and Medical Services annex of the NRP.

The Secretary of HHS directs and oversees HHS activities under ESF-8 through the Assistant Secretary for Public Health Emergency Preparedness (ASPHEP). These activities generally include activation of the Incident Management Team (IMT) within the Secretary's Operation Center (SOC), which serves as the focal point for coordination and communication within HHS and with the DHS and other departments and independent agencies. The ASPHEP serves as the Incident Manager. If warranted, the ASPHEP requests HHS Operating Divisions (OPDIVs) to provide individuals to serve on the IMT. OPDIV Emergency Operations Centers (EOCs) are activated in accordance with the magnitude of the response.

The scope and pace of an influenza pandemic may defy accurate prediction. **The disease may appear in many different parts of the Nation almost simultaneously, or disease may occur in only one or a few communities, and if not contained there, proceed to affect other communities.** In either case, the Secretary of HHS may have reason to exercise his authority under the Public Health Service Act to declare a Public Health Emergency prior to or essentially coincident with activation of the NRP.

appendix B: pandemic influenza background

Pandemics of influenza are extreme infectious disease outbreaks. Although many infectious disease outbreaks (e.g. Severe Acute Respiratory Syndrome [SARS], Ebola, HIV, or West Nile Virus) can cause devastation, these infections are typically limited in their spread to either localized areas or regions, or to at-risk populations. Pandemic influenza, by contrast, is an explosive global event in which most, if not all, populations worldwide are at risk for infection and illness. In past pandemics, influenza viruses have spread worldwide within months and are expected to spread even more quickly today given modern travel patterns.

It is the sheer scope of influenza pandemics, with their potential to rapidly spread and overwhelm societies and cause illnesses and deaths among all age groups, which distinguishes pandemic influenza from other emerging infectious disease threats and makes pandemic influenza one of the most feared emerging infectious disease threats.

A. Influenza viruses

The agent of pandemic influenza is the influenza virus, which is also responsible for causing seasonal influenza, known by most persons as the flu. Seasonal influenza, a common disease characterized by symptoms such as fever, fatigue, body pain, headache, dry cough, and sore throat, affects large numbers of people each year. Although most people infected with flu recover, it is still responsible for approximately 36,000 deaths and 226,000 hospitalizations each year in the U.S.

Influenza viruses are negative-stranded RNA viruses that have been classified taxonomically as orthomyxoviruses; they are divided into two types: "A" and "B" viruses. Influenza type C is not known to cause disease in humans and so is not applicable to this discussion. The remarkable variation of influenza strains—particularly type A—and their ability to cause annual epidemics of respiratory illness of varying intensity and severity, continue to be the focus of intense investigation. Only type A viruses are known to cause pandemics. Type A viruses are further divided into subtypes based on the specific hemagglutinin (H) and neuraminidase (N) proteins on the virus surface. Currently, two subtypes of A viruses are in worldwide circulation in humans: H3N2 and H1N1. The emergence of both of these subtypes in the 20th century led to separate pandemics. For example, the 1918 pandemic resulted from the emergence and spread of the H1N1 virus while the 1968 pandemic was associated with the H3N2 virus. The 1957 pandemic was associated with the emergence and spread of the H2N2 virus; however, this virus subtype stopped circulating in 1968. **Influenza pandemics are believed to have occurred for at least 300 years at unpredictable intervals.**

Pandemic influenza ... is an explosive global event in which most, if not all, populations worldwide are at risk for infection and illness.

B. Why influenza pandemics occur

1. Drift and shift

An important feature of influenza viruses that helps to explain much of their epidemiological patterns is the ability and propensity of these viruses to modify (drift) or replace (shift) two key viral proteins, hemagglutinin and neuraminidase, on the viral surface. Because these proteins are the main targets for the immune system, changes in these proteins can have minor to profound effects on the antigenicity of influenza viruses.

a) Drift

Influenza viruses can change through antigenic drift, which is a process in which mutations to the virus genome produce changes in the viral H or N. Drift is a continuous ongoing process that results in the emergence of new strain variants. The amount of change can be subtle or dramatic, but eventually one of the new variant strains becomes dominant, usually for a few years, until a new variant emerges and replaces it. In essence, drift affects the influenza viruses that are already in worldwide circulation. This process allows influenza viruses to change and re-infect people repeatedly through their lifetime and is the reason the influenza virus strains in vaccine must be updated each year.

b) Shift

In contrast to drift, pandemic viruses arise through a process known as antigenic shift. In this process, the surface existing viral H and N proteins are not modified, but are replaced by significantly different H and Ns. Since influenza A viruses that bear new (or novel) H or H/N combinations are perceived by immune systems as new, most people do not have pre-existing antibody protection to these novel viruses. This is one of the reasons that pandemic viruses can have such severe impact on the health of populations.

C. Animal reservoirs

Novel influenza viruses occasionally emerge among humans as part of the natural ecology and biology of influenza viruses. Wild birds are considered the reservoir for influenza viruses because more influenza A subtypes (15) circulate among wild birds than humans or other animal species. Normally, animal influenza viruses do not infect humans. However, avian influenza viruses can sometimes cross this barrier and directly infect humans. This was demonstrated in 1997, when an outbreak of avian influenza A (H5N1) viruses infected both domestic poultry and humans in Hong Kong, leading to 18 hospitalizations and 6 deaths. Since then, other outbreaks of avian viruses (such as H9N2 in 1999, H7N2 in 2002, H7N7 in 2003, and H5N1 again in 2004) have occurred and been found to directly infect people. Fortunately, these avian viruses lacked the ability to spread easily from person-to-person and therefore did not precipitate larger outbreaks or a pandemic.

Pandemic viruses can also arise when some of the genes from animal influenza viruses mix or reassort with some of the genes from human influenza viruses to create a new hybrid influenza virus. This can occur when a single animal (for example, a pig or possibly a person) is simultaneously co-infected by both a human influenza virus and an avian influenza virus. In this situation, genes from the human and avian viruses can reassort and create a virus with the surface proteins derived from the avian virus (hence, creating a new subtype) and the internal proteins derived from the human virus, enhancing the transmissibility of the hybrid virus. The process of reassortment is not theoretical. Reassorted viruses have been frequently identified and are thought to have been responsible for the 1957 and 1968 pandemic viruses.

D. Distinguishing pandemic from seasonal influenza

Several epidemiological features distinguish pandemic influenza from seasonal influenza. Pandemics of influenza are unusual events and their timing cannot be predicted. For example, only three pandemics occurred in the 20th century (1918, 1957, and 1968). The infrequency and unpredictable timing of these events is explained by the fact that influenza pandemics occur only when a new (or novel) influenza A virus emerges and spreads globally. By definition, most people have never been exposed to these viruses and therefore are susceptible to infection by them. In contrast, seasonal influenza virus strain variants are modified versions of influenza A viruses that are already in widespread circulation. Therefore, there is usually some level of pre-existing immunity to strain variants. Because of the frequent appearance of new variants, virus strains contained in seasonal interpandemic trivalent influenza vaccines must be updated annually.

Influenza pandemics occur only when a new (or novel) influenza A virus emerges and spreads globally.

It is clear that pandemic influenza has the potential to pose disease control challenges unmatched by any other natural or intentional infectious disease event.

E. Impact of influenza and influenza pandemics

An annual influenza season in the U.S., on average, results in approximately 36,000 deaths, 226,000 hospitalizations, and between $1 billion and $3 billion in direct costs for medical care. This impact occurs because influenza infections result in secondary complications such as pneumonia, dehydration, and worsening of chronic lung and heart problems. Despite the severity of influenza epidemics, it is sobering to understand that the effects of seasonal influenza are moderated because most individuals have some underlying degree of immunity to recently circulating influenza viruses either from previous infections or from vaccination.

It is clear that pandemic influenza has the potential to pose disease control challenges unmatched by any other natural or intentional infectious disease event. Pandemic influenza viruses have demonstrated their ability to spread worldwide within months, or weeks, and to cause infections in all age groups. While the ultimate number of infections, illnesses, and deaths is unpredictable, and could vary tremendously depending on multiple factors, it is nonetheless certain that without adequate planning and preparations, an influenza pandemic in the 21st century has the potential to cause enough illnesses to overwhelm current public health and medical care capacities at all levels, despite the vast improvements made in medical technology during the 20th century.

Certain modern trends could increase the potential for pandemics to cause more illnesses and deaths than occurred in earlier pandemics:

- First, the global population is larger and increasingly urbanized, allowing viruses to be transmitted within populations more easily.
- Second, levels of international travel are much greater than in the past, allowing viruses to spread globally more quickly than in the past.
- Third, populations in many countries consist of increasing numbers of elderly persons and those with chronic medical conditions, thus increasing the potential for more complicated illnesses and deaths to occur.

This combination of factors suggests that the next pandemic may lead to more illnesses occurring more quickly than in the past, overwhelming countries and health systems that are not adequately prepared.

The 1957 pandemic, during an era with much less globalization, spread to the U.S. within 4-5 months of its detection in China, and the 1968 pandemic spread to the U.S. from Hong Kong within 2-3 months. As was amply demonstrated by the SARS outbreak, modern travel patterns may significantly reduce the time needed for pandemic influenza viruses to spread globally to a few months or even weeks. The major implication of such rapid spread of an infectious disease is that many, if not most, countries will have minimal time to implement preparations and responses once pandemic viruses have begun to spread. While SARS infections spread quickly to multiple countries, the epidemiology and transmission modes of the SARS virus greatly helped to contain the spread of this infection in 2003, along with quarantine, isolation, and other control measures. Fortunately, no widespread community transmission took place. By contrast, because influenza spreads more rapidly between

Table B–1: Effects of Past Pandemics on the U.S.

Pandemic	Estimated U.S. Deaths	Influenza A Strain	Populations at greatest risk
1918-1919	500,000	H1N1	Young, healthy adults
1957-1958	70,000	H2N2	Infants, elderly
1968-1969	34,000	H3N2	Infants, elderly

people and can be transmitted by those who are infected but do not yet have symptoms, the spread of pandemic influenza to multiple countries is expected to lead to the near simultaneous occurrence of multiple community outbreaks in an escalating fashion. No other infectious disease threat, whether natural or engineered, poses the same current threat for causing increases in infections, illnesses, and deaths so quickly in the U.S. and worldwide.

F. H5N1 avian influenza

Although it is unpredictable when the next pandemic will occur and what strain may cause it, the continued and expanded spread of a highly pathogenic—and now endemic—avian H5N1 virus across much of eastern Asia, Russia, and eastern Europe represents a significant pandemic threat. Human avian H5N1 influenza infection was first recognized in 1997 when it infected 18 people in Hong Kong, causing 6 deaths. Concern has increased in recent years as avian H5N1 infections have killed poultry flocks in countries throughout Asia and in parts of Europe. Since 2003, over 100 human H5N1 cases have been diagnosed in Thailand, Vietnam, Cambodia, and Indonesia. The H5N1 virus circulating in Asia has raised concerns about the potential for a pandemic because:

- The avian H5N1 virus is widespread and endemic in much of Asia with spread to Russia and Europe.
- The avian H5N1 virus is becoming more deadly in a growing number of bird species and mammals.
- Wild birds and domestic ducks may be infected asymptomatically, providing a reservoir for infection of other domestic poultry species.
- The virus is able to transmit directly from birds to some mammals and in some circumstances to people.
- There is sporadic spread directly from animals to humans with suspected human-to-human transmission in rare instances.
- Genetic studies confirm that H5N1, like other influenza viruses, is continuing to change and evolve.

While H5N1 is the greatest current pandemic threat, other avian influenza subtypes have also infected people in recent years. In 1999, H9N2 infections were identified in Hong Kong; in 2003, H7N7 infections occurred in the Netherlands; and in 2004, H7N3 infections occurred in Canada. Such outbreaks have the potential to give rise to the next pandemic, reinforcing the need for continued surveillance and ongoing vaccine development efforts against these strains.

appendix C: WHO pandemic phases

In 1999, the World Health Organization (WHO) Secretariat published guidance for pandemic influenza and defined the phases of a pandemic. Updated guidance was published in 2005 to redefine these phases. This schema is designed to provide guidance to the international community and to national governments on preparedness and response for pandemic threats and pandemic disease. Compared with the 1999 phases, the new definitions place more emphasis on pre-pandemic phases when pandemic threats may exist in animals or when new influenza virus subtypes infect people but do not spread efficiently. Recognizing that distinctions between the two interpandemic phases and the three pandemic alert phases may be unclear, the WHO Secretariat proposes to base classification on assessment of risk based on a range of scientific and epidemiological data.

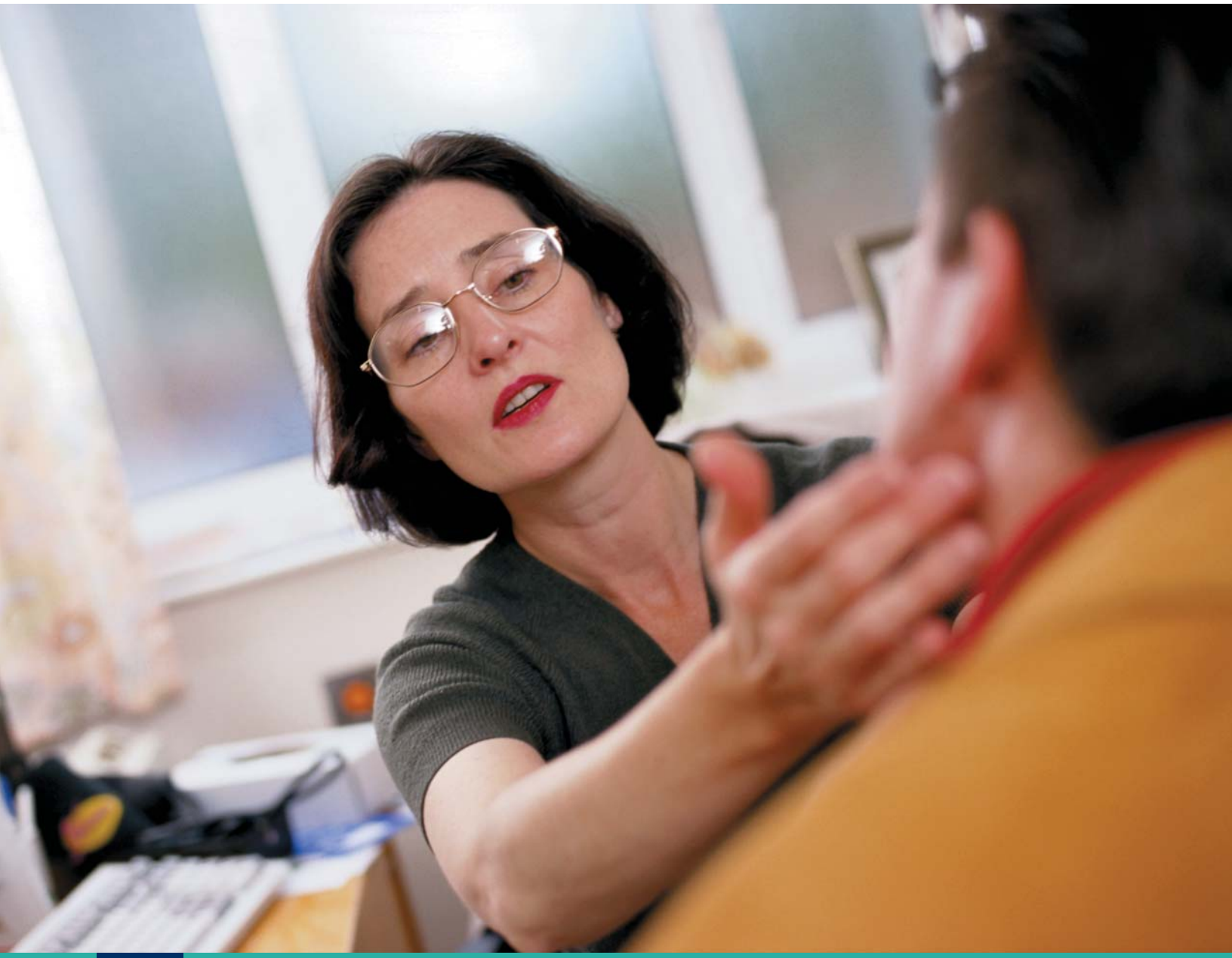
Table C–1: Summary of WHO Global Pandemic Phases (WHO Global Influenza Preparedness Plan, 2005)

Interpandemic Period	
Phase 1.	No new influenza virus subtypes have been detected in humans. An influenza virus subtype that has caused human infection may be present in animals. If present in animals, the risk of human infection or disease is considered to be low
Phase 2.	No new influenza virus subtypes have been detected in humans. However, a circulating animal influenza virus subtype poses a substantial risk of human disease
Pandemic Alert Period	
Phase 3.	Human infection(s) with a new subtype but no human-to-human spread or at most rare instances of spread to a close contact
Phase 4.	Small cluster(s) with limited human-to-human transmission but spread is highly localized, suggesting that the virus is not well adapted to humans
Phase 5.	Larger cluster(s) but human-to-human spread is still localized, suggesting that the virus is becoming increasingly better adapted to humans but may not yet be fully transmissible (substantial pandemic risk)
Pandemic Period	
Phase 6.	Pandemic phase: increased and sustained transmission in the general population
Postpandemic Period	
Return to the Interpandemic Period (Phase 1)	

[1] http://www.who.int/csr/resources/publications/influenza/whocdscsredc991.pdf

[2] http://www.who.int/csr/resources/publications/influenza/WHO_CDS_CSR_GIP_2005_5.pdf

Recognizing that at any pandemic phase, national situations will differ based on whether a country is affected or not affected by the novel influenza subtype, the WHO Secretariat recommends "national subdivisions" of phases based on whether a country is experiencing disease or has extensive trade and travel links with an affected country. National subdivisions of phases will be designated by national authorities. In the United States, pandemic phases will be defined based on the global phase and determined by the Secretary of Health and Human Services. During the pandemic phase, additional subdivisions may be defined based on the extent of disease. In actual practice, the distinction between the various phases of pandemic influenza may be blurred or occur in a matter of hours, again underscoring the need for flexibility.



appendix D: NVAC/ACIP recommendations for prioritization of pandemic influenza vaccine and NVAC recommendations on pandemic antiviral drug use

Advisory Committee recommendations ... provide guidance for planning purposes and form the basis for further discussion of how to equitably allocate medical countermeasures that will be in short supply early in an influenza pandemic.

Advisory Committee recommendations are presented in this report to provide guidance for planning purposes and to form the basis for further discussion of how to equitably allocate medical countermeasures that will be in short supply early in an influenza pandemic.

Two federal advisory committees, the Advisory Committee on Immunization Practices (ACIP) and the National Vaccine Advisory Committee (NVAC), provided recommendations to the Department of Health and Human Services on the use of vaccines and antiviral drugs in an influenza pandemic.

Although the advisory committees considered potential priority groups broadly, the main expertise of the members was in health and public health. The primary goal of a pandemic response considered was to decrease health impacts including severe morbidity and death; secondary pandemic response goals included minimizing societal and economic impacts. However, as other sectors are increasingly engaged in pandemic planning, additional considerations may arise. The advisory committee reports explicitly acknowledge the importance of this, for example highlighting the priority for protecting critical components of the military. Finally, HHS has recently initiated outreach to engage the public and obtain a broader perspective into decisions on priority groups for pandemic vaccine and antiviral drugs. Though findings of the outreach are preliminary, a theme that has emerged is the importance of limiting the effects of a pandemic on society by preserving essential societal functions.

Based on this guidance, state, local, and tribal implementation plans should be developed to 1) include more specific definitions of the priority groups (e.g., which functions are indeed critical to maintaining continuity) and their size; 2) define how persons in these groups will be identified; and 3) establish strategies for effectively and equitably delivering vaccines and antiviral drugs to these populations. The committees acknowledged that further work is needed, in particular, to identify the functions that must be preserved to maintain effective services and critical infrastructures and to identify the groups that should be protected to achieve this goal. The committees also acknowledge that the specific composition of some priority groups may differ between states or localities based on their needs and that priority groups should be reconsidered when a pandemic occurs and information is obtained on its epidemiology and impacts.

On July 19, 2005, ACIP and NVAC voted unanimously in favor of the vaccine priority recommendations summarized in Table D-1. These votes followed deliberations of a joint Working Group of the two committees, which included as consultants representatives of public and private sector stakeholder organizations and academic experts. There was limited staff level participation from DoD, DHS, and VA. Several ethicists also served as consultants to the Working Group.

A. Critical assumptions

The recommendations summarized in Table D-1 were based on the following critical assumptions:

- **Morbidity and mortality.** The greatest risk of hospitalization and death—as during the 1957 and 1968 pandemics and annual influenza—will be in infants, the elderly, and those with underlying health conditions. In the 1918 pandemic, most deaths occurred in young adults, highlighting the need to reconsider the recommendations at the time of the pandemic based on the epidemiology of disease.
- **Healthcare system.** The healthcare system will be severely taxed if not overwhelmed due to the large number of illnesses and complications from influenza requiring hospitalization and critical care. CDC models estimate increases in hospitalization and intensive care unit demand of more than 25% even in a moderate pandemic.
- **Workforce.** During a pandemic wave in a community, between 25% and 30% of persons will become ill during a 6 to 8 week outbreak. Among working-aged adults, illness attack rates will be lower than in the community as a whole. A CDC model suggests that at the peak of pandemic disease, about 10% of the workforce will be absent due to illness or caring for an ill family member. Impacts will likely vary between communities and work sites and may be greater if significant absenteeism occurs because persons stay home due to fear of becoming infected.
- **Critical infrastructure.** Only limited information was available from which to assess potential impacts on critical infrastructure sectors such as transportation and utility services. Because of changes in business practices and the complexity of networks, information from prior pandemics was not considered applicable.
- **Vaccine production capacity.** The U.S.-based vaccine production capacity was assumed at 3 to 5 million 15µg doses per week with 3 to 6 months needed before the first doses are produced. Two doses per person were assumed to be required for protection. Subsequent results of an NIH clinical trial of influenza A (H5N1) vaccine suggest that higher doses of antigen will be needed to elicit a good immune response; thus, the assumptions made by the committee could potentially substantially exceed the amount of vaccine that would be produced.

Table D–1: Vaccine Priority Group Recommendations*

Tier	Subtier	Population	Rationale
1	A	■ Vaccine and antiviral manufacturers and others essential to manufacturing and critical support (~40,000) ■ Medical workers and public health workers[3] who are involved in direct patient contact, other support services essential for direct patient care, and vaccinators (8-9 million)	■ Need to assure maximum production of vaccine and antiviral drugs ■ Healthcare workers are required for quality medical care (studies show outcome is associated with staff-to-patient ratios). There is little surge capacity among healthcare sector personnel to meet increased demand.
	B	■ Persons ≥ 65 years with 1 or more influenza high-risk conditions, not including essential hypertension (approximately 18.2 million) ■ Persons 6 months to 64 years with 2 or more influenza high-risk conditions, not including essential hypertension (approximately 6.9 million) ■ Persons 6 months or older with history of hospitalization for pneumonia or influenza or other influenza high-risk condition in the past year (740,000)	■ These groups are at high risk of hospitalization and death. Excludes elderly in nursing homes and those who are immunocompromised and would not likely be protected by vaccination
	C	■ Pregnant women (approximately 3.0 million) ■ Household contacts of severely immunocompromised persons who would not be vaccinated due to likely poor response to vaccine (1.95 million with transplants, AIDS, and incident cancer x 1.4 household contacts per person = 2.7 million persons) ■ Household contacts of children <6 month olds (5.0 million)	■ In past pandemics and for annual influenza, pregnant women have been at high risk; vaccination will also protect the infant who cannot receive vaccine. ■ Vaccination of household contacts of immunocompromised and young infants will decrease risk of exposure and infection among those who cannot be directly protected by vaccination.
	D	■ Public health emergency response workers critical to pandemic response (assumed one-third of estimated public health workforce=150,000) ■ Key government leaders	■ Critical to implement pandemic response such as providing vaccinations and managing/monitoring response activities ■ Preserving decision-making capacity also critical for managing and implementing a response

[3] This is inclusive of federal healthcare providers to Indian nations and tribes.

Table D–1. Continued

Tier	Subtier	Population	Rationale
2	A	■ Healthy 65 years and older (17.7 million) ■ 6 months to 64 years with 1 high-risk condition (35.8 million) ■ 6-23 months old, healthy (5.6 million)	■ Groups that are also at increased risk but not as high risk as population in Tier 1B
	B	■ Other public health emergency responders (300,000 = remaining two-thirds of public health work force) ■ Public safety workers including police, fire, 911 dispatchers, and correctional facility staff (2.99 million) ■ Utility workers essential for maintenance of power, water, and sewage system functioning (364,000) ■ Transportation workers transporting fuel, water, food, and medical supplies as well as public ground public transportation (3.8 million) ■ Telecommunications/IT for essential network operations and maintenance (1.08 million)	■ Includes critical infrastructure groups that have impact on maintaining health (e.g., public safety or transportation of medical supplies and food); implementing a pandemic response; and on maintaining societal functions
3		■ Other key government health decision-makers (estimated number not yet determined) ■ Funeral directors/embalmers (62,000)	■ Other important societal groups for a pandemic response but of lower priority
4		■ Healthy persons 2-64 years not included in above categories (179.3 million)	■ All persons not included in other groups based on objective to vaccinate all those who want protection

*The committee focused its deliberations on the U.S. civilian population. ACIP and NVAC recognize that Department of Defense needs should be highly prioritized. DoD Health Affairs indicates that 1.5 million service members would require immunization to continue current combat operations and preserve critical components of the military medical system. Should the military be called upon to support civil authorities domestically, immunization of a greater proportion of the total force will become necessary. These factors should be considered in the designation of a proportion of the initial vaccine supply for the military.

Other groups also were not explicitly considered in these deliberations on prioritization. These include American citizens living overseas, non-citizens in the U.S., and other groups providing national security services such as the border patrol and customs service.

B. Definitions and rationales for priority groups

1. Healthcare workers and essential healthcare support staff

a) Definition

Healthcare workers (HCW) with direct patient contact (including acute-care hospitals, nursing homes, skilled nursing facilities, urgent care centers, physician's offices, clinics, home care, blood collection centers, and EMS) and a proportion of persons working in essential healthcare support services needed to maintain healthcare services (e.g. dietary, housekeeping, admissions, blood collection center staff, etc.). Also included are healthcare workers in public health with direct patient contact, including those who may administer vaccine or distribute influenza antiviral medications, and essential public health support staff for these workers.

b) Rationale

The pandemic is expected to have substantial impact on the healthcare system with large increases in demand for healthcare services placed on top of existing demand. HCW will be treating influenza-infected patients and will be at risk of repeated exposures. Further, surge capacity in this sector is low. To encourage continued work in a high-exposure setting and to help lessen the risk of healthcare workers transmitting influenza to other patients and HCW family members, this group was highly prioritized. In addition, increases in bed/nurse ratios have been associated with increases in overall patient mortality. Thus, substantial absenteeism may affect overall patient care and outcomes.

2. Groups at high risk of influenza complications

a) Definition

Persons 2-64 years with a medical condition for which influenza vaccine is recommended and all persons 6-23 months and 65 years and older. Excludes nursing home residents and severely immunocompromised persons who would not be expected to respond well to vaccination.

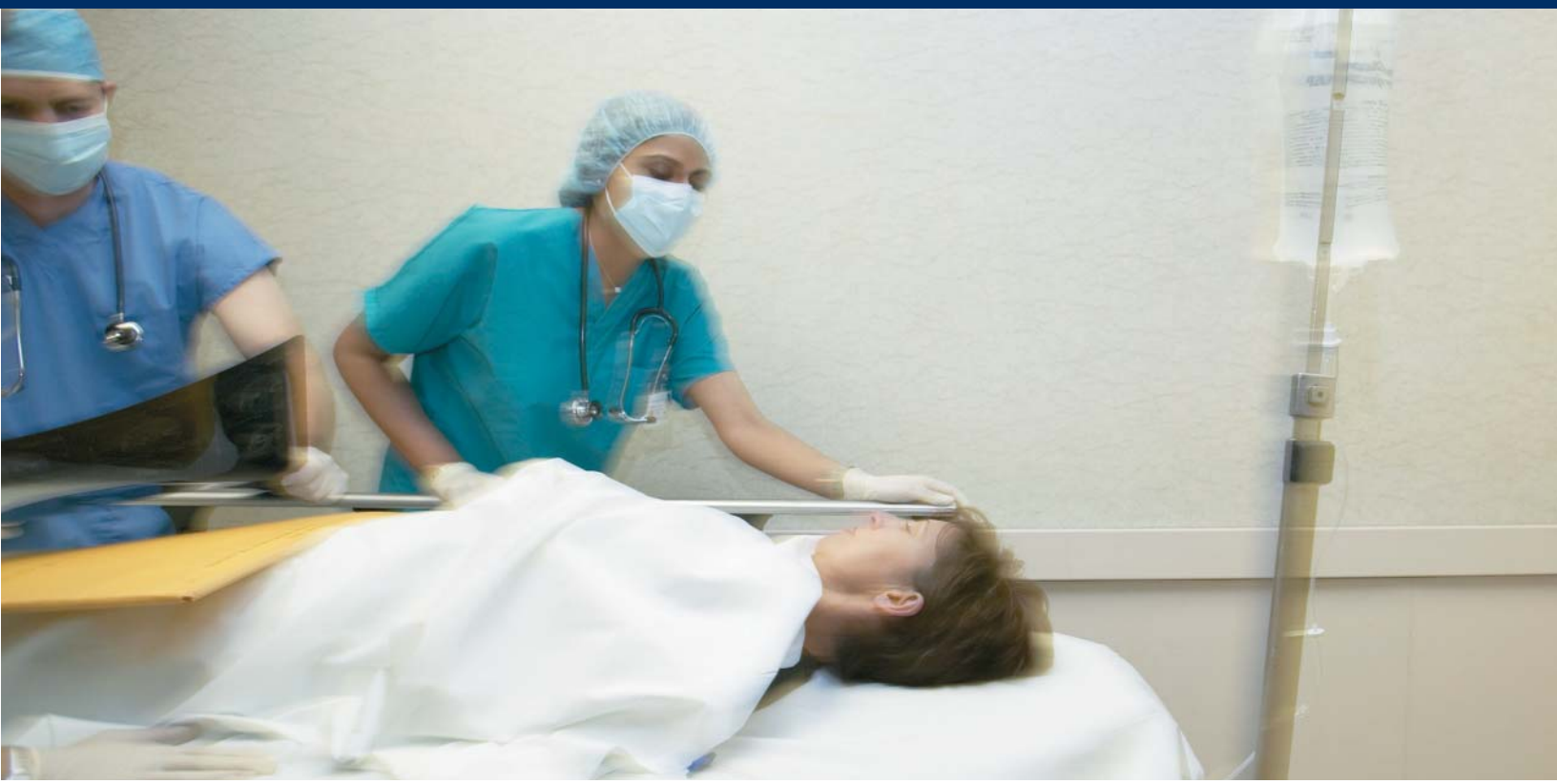
b) Rationale

These groups were prioritized based on their risk of influenza-related hospitalization and death and also their likelihood of vaccine response. Information from prior pandemics was used whenever possible, but information from interpandemic years was also considered. Nursing home residents and severely immunocompromised persons would be prioritized for antiviral treatment and/or prophylaxis and vaccination of healthcare workers and household contacts who are most likely to transmit influenza to these high risk groups.

3. Critical infrastructure

a) Definitions and rationale

Those critical infrastructure sectors that fulfill one or more of the following criteria: have increased demand placed on them during a pandemic, directly support reduction in deaths and hospitalization; function is critical to support the healthcare sector and other emergency services, and/or supply basic



necessities and services critical to support of life and healthcare or emergency services. Groups included in critical infrastructure are needed to respond to a pandemic and to minimize morbidity and mortality, and include the following sectors:

- Persons directly involved with influenza vaccine and antiviral medication manufacturing and distribution and essential support services and suppliers (e.g., growers of pathogen-free eggs for growth of vaccine virus) production activities
- Key government leaders and health decision-makers who will be needed to quickly move policy forward on pandemic prevention and control efforts
- Public safety workers (firefighters, police, and correctional facility staff, including dispatchers) are critical to maintaining social functioning and order and will contribute to a pandemic response, for example by ensuring order at vaccination clinics and responding to medical emergencies
- Utility service workers (water, power, and sewage management) are prioritized as the services they provide are also essential to the healthcare system as well as to preventing additional illnesses from lack of these services unrelated to a pandemic.
- Transportation workers who maintain critical supplies of food, water, fuel, and medical equipment and who provide public transportation, which is essential for provision of medical care and transportation of healthcare workers to work and transportation of ill persons for care
- Telecommunication and information technology services critical for maintenance and repairs of these systems are also essential as these systems are now critical for accessing and delivering medical care and in support of all other critical infrastructure.
- Mortuary services will be substantially impacted due to the increased numbers of deaths from a pandemic and the fact that impact will be high in the elderly, a growing segment of the population

4. Public health emergency response workers

a) Definition

This group includes persons who do not have direct patient care duties, but who are essential for surveillance for influenza, assessment of the pandemic impact, allocation of public health resources for the pandemic response, development and implementation of public health policy as part of the response, and development of guidance as the pandemic progresses.

b) Rationale

Persons in this sector have been critical for past influenza vaccine pandemics and influenza vaccine shortages and little surge capacity may be available during a public health emergency such as a pandemic.

5. Persons in skilled nursing facilities

a) Definition

Patients residing in skilled nursing facilities. Not included in this group are persons in other residential settings (e.g., assisted living) who are more likely to be mobile, in a setting that is less closed, and have decentralized healthcare.

b) Rationale

This group was not prioritized for vaccine because of the medical literature finding poor response to vaccination and occurrence of outbreaks even in the setting of high vaccination rates. Other studies have suggested that vaccination of healthcare workers may be a more effective strategy to prevent influenza in this group. Further, surveillance for influenza can be conducted in this group and antiviral medications used widely for prophylaxis and treatment. Ill visitors and staff should also be restricted from visiting nursing home facilities during outbreaks of pandemic influenza.

This strategy for pandemic influenza vaccine differs from the interpandemic vaccination strategy of aggressively vaccinating nursing home residents. The rationale considers several factors: 1) these populations are less likely to benefit from vaccine than other groups who are also at high risk; 2) other prevention strategies feasible for this group are not possible among other high-risk groups; 3) the overall morbidity and mortality from pandemic is likely to severely impact other groups of persons who would be expected to have a better response to the vaccine; and 4) a more severe shortage of vaccine is anticipated.

6. Severely immunocompromised persons

a) Definition

Persons who are undergoing or who have recently undergone bone marrow transplantation and others with severe immunodeficiency (e.g., AIDS patients with CD4 counts <50, children with SCID syndrome, recent bone marrow transplant patients). The numbers of persons in these categories is likely much smaller than the anticipated number assumed in tiering above, but sources for more specific estimates have not been identified.

b) Rationale

These groups have a lower likelihood of responding to influenza vaccination. Thus, strategies to prevent severe influenza illness in this group should include vaccination of healthcare workers and household contacts of severely immunocompromised persons and use of antiviral medications. Consideration should be given to prophylaxis of severely immunocompromised persons with influenza antivirals and early antiviral treatment should they become infected.

7. Children <6 months of age

a) Rationale

Influenza vaccine is poorly immunogenic in children <6 months and the vaccine is currently not recommended for this group. In addition, influenza antiviral medications are not FDA-approved for use in children <1 year old. Thus, vaccination of household contacts and out-of-home caregivers of children <6 months is recommended to protect this high-risk group.

C. Other discussion

There was substantial discussion on priority for children. Four potential reasons were raised for making vaccination of children a priority:

- At the public engagement session, many participants felt that children should have high priority for vaccination.
- Children play a major role in transmitting infection, and vaccinating this group could slow the spread of disease and indirectly protect others.
- Children have strong immune systems and will respond well to vaccine whereas vaccination of the elderly and those with illnesses may be less effective.
- Some ethical frameworks would support a pediatric priority.

ACIP and NVAC did not make children a priority (other than those included in tiers, because of their underlying diseases [Tiers 1B and 2A] or as contacts of high-risk persons [Tier 1C]) for several reasons:

- Healthy children have been at low risk for hospitalization and death in prior pandemics and during annual influenza seasons.
- It is uncertain whether vaccination of children will decrease transmission and indirectly protect others. Studies that show this impact or mathematical models that predict it rely on high vaccination coverage that may not be possible to achieve given limited supplies in a pandemic.
- The committees recognize that this is an area for further scientific work; that children may be a good target population for live-attenuated influenza vaccine (FluMist®) if it is available; and that education of the public will be needed to provide the rationale for the recommendations.

NVAC recognizes that recommendations [for antiviral drug use] will need to be reconsidered at the time of a pandemic when information on the available drug supply, epidemiology of disease, and impacts on society are known.

The committee considered the primary goal of a pandemic response to decrease health impacts including severe morbidity and death. Minimizing societal and economic impacts were considered secondary and tertiary goals.

NVAC RECOMMENDATIONS ON PANDEMIC ANTIVIRAL DRUG USE

On July 19, 2005, NVAC voted unanimously in favor of the antiviral drug use priority recommendations described here and summarized in Table D-2. These votes followed deliberations of a Working Group, which included as consultants representatives of public and private sector stakeholder organizations and academic experts. There was limited staff level participation from DoD, DHS, and VA. Several ethicists also served as consultants to the Working Group.

The recommendations were made considering pandemic response goals, assumptions on the impacts of a pandemic, and after thorough review of past pandemics, annual influenza disease, data on antiviral drug impacts, and recommendations for pandemic vaccine use.

Recommendations were made to guide planning needed for effective implementation at state and local levels. The committee recognizes that recommendations will need to be reconsidered at the time of a pandemic when information on the available drug supply, epidemiology of disease, and impacts on society are known.

The committee considered the primary goal of a pandemic response to decrease health impacts including severe morbidity and death. Minimizing societal and economic impacts were considered secondary and tertiary goals.

A. Critical assumptions

Assumptions regarding groups at highest risk during a pandemic and impacts on the healthcare system and other critical infrastructures are the same as those underlying the vaccine priority recommendations. Additional assumptions specific for antiviral drugs included:

- Treatment with a neuraminidase inhibitor (oseltamivir [Tamiflu®] or zanamivir [Relenza®]) will be effective in decreasing risk of pneumonia, will decrease hospitalization by about half (as shown for interpandemic influenza), and will also decrease mortality.
- Antiviral resistance to the adamantanes (amantadine and rimantadine) may limit their use during a pandemic.
- The primary source of antiviral drugs for a pandemic response will be the supply of antiviral drugs that have been stockpiled. Before annual influenza seasons about 2 million treatment courses of oseltamivir are available in the U.S. U.S.-based production of oseltamivir is being established; expected capacity is projected at about 1.25 million courses per month.
- Treating earlier after the onset of disease is most effective in decreasing the risk of complications and shortening illness duration. Generally, treatment should be given within the first 48 hours.
- Assumptions for the amount of antiviral drug needed for defined priority groups is based on the population in those groups and assumptions that 35% of persons in the priority groups will have influenza-like illness and 75% will present within the first 48 hours and be eligible for treatment. For persons admitted to the hospital, the committee assumed that 80% would be treated, as the 48-hour limit may sometimes be relaxed in more ill patients.
- Unlike vaccines, where each tier would be protected in turn as more vaccine is produced, for antiviral drugs, the number of priority groups that can be covered would be known at the start of the pandemic based on the amount of drug that is stockpiled. Additional supply that would become available during the pandemic could provide some flexibility.

Table D–2: Antiviral Drug Priority Group Recommendations*

	Group	Estimated population (millions)	Strategy**	# Courses (millions)		Rationale
				For target group	Cumulative	
1	Patients admitted to hospital***	10.0	T	7.5	7.5	Consistent with medical practice and ethics to treat those with serious illness and who are most likely to die
2	Health care workers (HCW) with direct patient contact and emergency medical service (EMS) providers[4]	9.2	T	2.4	9.9	Healthcare workers are required for quality medical care. There is little surge capacity among healthcare sector personnel to meet increased demand.
3	Highest risk outpatients—immunocompromised persons and pregnant women	2.5	T	0.7	10.6	Groups at greatest risk of hospitalization and death; immunocompromised cannot be protected by vaccination.
4	Pandemic health responders (public health, vaccinators, vaccine and antiviral manufacturers), public safety (police, fire, corrections), and government decision-makers	3.3	T	0.9	11.5	Groups are critical for an effective public health response to a pandemic.
5	Increased risk outpatients—young children 12-23 months old, persons ≥ 65 yrs old, and persons with underlying medical conditions	85.5	T	22.4	33.9	Groups are at high risk for hospitalization and death.
6	Outbreak response in nursing homes and other residential settings	NA	PEP	2.0	35.9	Treatment of patients and prophylaxis of contacts is effective in stopping outbreaks; vaccination priorities do not include nursing home residents
7	HCWs in emergency departments, intensive care units, dialysis centers, and EMS providers	1.2	P	4.8	40.7	These groups are most critical to an effective healthcare response and have limited surge capacity. Prophylaxis will best prevent absenteeism.
8	Pandemic societal responders (e.g., critical infrastructure groups as defined in the vaccine priorities) and HCW without direct patient contact	10.2	T	2.7	43.4	Infrastructure groups that have impact on maintaining health, implementing a pandemic response, and maintaining societal functions
9	Other outpatients	180	T	47.3	90.7	Includes others who develop influenza and do not fall within the above groups
10	Highest risk outpatients	2.5	P	10.0	100.7	Prevents illness in the highest risk groups for hospitalization and death.
11	Other HCWs with direct patient contact	8.0	P	32.0	132.7	Prevention would best reduce absenteeism and preserve optimal function.

[4] This is inclusive of Federal healthcare providers to Indian Nations and Tribes.

B. Definitions and rationale for draft priority groups

1. Persons admitted to hospital with influenza infection

a) Definition

Persons admitted to acute care facilities (traditional or non-traditional with a clinical diagnosis of influenza; laboratory confirmation not required). Excludes persons admitted for a condition consistent with a bacterial superinfection (e.g., lobar pneumonia developing late after illness onset) or after viral replication and shedding has ceased (e.g., as documented by a negative sensitive antigen detection test)

b) Strategy

Treatment within 48 hours of system onset.

c) Rationale

This group is at greatest risk for severe morbidity and mortality. Although there are no data to document the impacts of antiviral drug treatment among persons who already suffer more severe influenza illness, benefit is biologically plausible in persons with evidence of ongoing virally-mediated pathology (e.g., diffuse pneumonia, ARDS). Providing treatment to those who are most ill is also consistent with standard medical practices, would be feasible to implement, and would be acceptable to the public.

d) Population size

The number of persons admitted to hospital in an influenza pandemic would vary substantially depending on the severity of the pandemic and on the ability to expand inpatient capacity, if needed.

e) Unresolved issues

More specific guidance should be provided to healthcare workers on implementing antiviral treatment, including when and when not to treat. In some persons with severe illness, the ability to take oral medication or its absorption may be important issues. For infants <1 year old admitted to hospital,

*The committee focused its deliberations on the domestic U.S. civilian population. NVAC recognizes that Department of Defense (DoD) needs should be highly prioritized. A separate DoD antiviral stockpile has been established to meet those needs. Other groups also were not explicitly considered in deliberations on prioritization. These include American citizens living overseas, non-citizens in the U.S., and other groups providing national security services such as the border patrol and customs service.

**Strategy: Treatment (T) requires a total of 10 capsules and is defined as 1 course. Post-exposure prophylaxis (PEP) also requires a single course. Prophylaxis (P) is assumed to require 40 capsules (4 courses) though more may be needed if community outbreaks last for a longer period.

***There are no data on the effectiveness of treatment at hospitalization. If stockpiled antiviral drug supplies are very limited, the priority of this group could be reconsidered based on the epidemiology of the pandemic and any additional data on effectiveness in this population.

decisions about whether to treat with antiviral drugs may depend on the child's age and potential risk versus benefit as the neuraminidase inhibitors are not licensed for use in infants. If possible, data on time from symptom onset to hospital admission, current use of antiviral drug treatment among inpatients, and its impacts should be collected during interpandemic influenza seasons.

2. Healthcare workers and emergency medical service providers who have direct patient contact

a) Definition

Persons providing direct medical services in inpatient and outpatient care settings. Includes doctors, nurses, technicians, therapists, EMS providers, laboratory workers, other care providers who come within 3 feet of patients with influenza, and persons performing technical support functions essential to quality medical care.

b) Strategy

Treatment within 48 hours of symptom onset.

c) Rationale

Maintaining high quality patient care is critical to reduce health impacts of pandemic disease and to prevent adverse outcomes from other health conditions that will present for care during the pandemic period. Treatment of healthcare providers will decrease absenteeism due to influenza illness and may decrease absenteeism from fear of becoming ill, given the knowledge that treatment can prevent serious complications of influenza. Good data exist documenting the impacts of early treatment on duration of illness and time off work, and on the occurrence of complications such as lower respiratory infections. Treating healthcare providers is feasible to implement, especially for inpatient care providers who can be provided drugs through the occupational health clinic. It also would be acceptable to the public, who would recognize the importance of maintaining quality healthcare and would understand that persons with direct patient contact are putting themselves at increased risk.

d) Population size

There are about 12.6 million persons designated as healthcare workers by the Bureau of Labor Statistics and about 820,000 EMS providers. Among HCWs, two-thirds are estimated to provide direct patient care services.

e) Unresolved issues

Further work is needed to hone definitions and estimate population sizes. Implementation issues include the approach to identifying healthcare providers who would be eligible for treatment and where the treatment would be provided, particularly for outpatient care providers.

3. Outpatients at highest risk for severe morbidity or mortality from influenza infection

a) Definition

The Advisory Committee on Immunization Practices defines groups at high risk (or increased risk) of complications from influenza infection during annual outbreaks based on age (6-23 months and >65 years) and underlying illnesses. Among this population of about 88 million persons, some can be identified who are at highest risk of severe disease and death. These include persons with hematopoetic stem cell transplants (HSCT) and solid organ transplants; those with severe immunosuppression due to cancer therapy or hematological malignancy; persons receiving immunosuppressive therapy for other illnesses (e.g., rheumatoid arthritis); persons with HIV infection and a CD4 count <200; persons on dialysis; and women who are in the second or third trimester of pregnancy.

b) Strategy

Treatment within 48 hours of symptom onset.

c) Rationale

Of the large group of persons who are at increased risk of severe disease or death from influenza, these groups represent the population at highest risk and who are least likely to be protected by vaccination. Studies show that neuraminidase inhibitor therapy decreases complications and hospitalizations from influenza in high-risk persons and one unpublished study shows a significant decrease in mortality among patients who have undergone a hematopoteic stem cell transplant.

d) Population size

About 150,000 persons have had an HSCT or solid organ transplant. Assuming that the period of severe immunosuppression after a cancer diagnosis lasts for 1 year, the population targeted with non-skin, non-prostate cancers would equal the incidence of about 1.35 million persons. Based on a birth cohort of 4.1 million, a 28-week risk period during the second and third trimesters, and an 8-week pandemic outbreak in a community, there would be about 400,000 pregnant women included in this risk group. Further work is needed to estimate the size of other immunosuppressed groups.

e) Unresolved issues

Specific definition of included groups and population sizes.

4. Pandemic health responders, public safety workers, and key government decision-makers

a) Definition

Public health responders include those who manufacture vaccine and antiviral drugs; persons working at health departments who are not included as healthcare workers; and those who would be involved in implementing pandemic vaccination or other response components. Public safety workers include police, fire, and corrections personnel. Key government decision-makers include chief executives at federal, state, and local levels.

b) Strategy

Treatment within 48 hours of symptom onset.

c) Rationale

Preventing adverse health outcomes and social and economic impacts in a pandemic depend on the ability to implement an effective pandemic response. Early treatment of pandemic responders will minimize absenteeism and ensure that vaccination and other critical response activities can be maintained. Implementing early treatment for public health workers and vaccine manufacturers is feasible at workplace settings. Public safety workers prevent intentional and unintentional injuries and death, are critical to maintaining social functioning, and will contribute to a pandemic response, for example by ensuring order at vaccination clinics. A small number of decision-makers at federal, state, and local levels are needed to for an effective pandemic response.

d) Population size

An estimated 40,000 workers who produce pandemic vaccine and antiviral drugs in the U.S.; ~300,000 public health workers who would not be included in the HCW category; 3 million public safety workers; and a small number of government decision-makers.

e) Unresolved issues

Need to define the exact composition and size of this group.

5. Outpatients at increased risk of severe morbidity or mortality from influenza

a) Definition

For planning purposes, this group would include those currently designated as high-risk groups, except for those who have been categorized as being at highest-risk and included in a separate category. This increased-risk group includes persons 6-23 months and >65 years old, or who have underlying illnesses defined by the ACIP as associated with increased risk. Definition of this group may change based on the epidemiology of the pandemic.

b) Strategy

Treatment within 48 hours of symptom onset.

c) Rationale

Early treatment has been shown to significantly decrease lower respiratory infections and to reduce the rate of hospitalization in elderly and high-risk populations. By extrapolation and based on the results of one small uncontrolled study, significant reductions of mortality can be expected as well. As these risk groups are familiar to the public given recommendations for annual vaccination, communication would be easy and acceptability high.

d) Population size

About 85.5 million persons are included in this group. Although all are at increased risk of annual influenza compared with the healthy under-65 year old population, there are different levels of increased risk for severe complications and death within this category. Further stratification may be possible based on several parameters including number of underlying conditions; recent hospitalization for a high-risk condition, pneumonia, or influenza; and age.

e) Unresolved issues

Stratifying this group into those at greater and lesser risk may be important if antiviral supplies are limited. Implementing treatment will be challenging given that it should be provided at the initial point of care to accrue the greatest benefit from early therapy.

6. Outbreak control

a) Definition

Use of antiviral drugs to support public health interventions in closed settings where an outbreak of pandemic influenza is occurring.

b) Strategy

Treatment of cases and post-exposure prophylaxis of contacts (once daily antiviral medication for 10 days).

c) Rationale

Influenza outbreaks in nursing homes are associated with substantial mortality and morbidity. Nursing home residents also are less likely to respond to vaccination. Post-exposure prophylaxis has been shown to be effective in stopping influenza outbreaks in closed settings.

d) Population size

The number of outbreaks that may occur during a pandemic is unclear. Measures should be implemented to prevent outbreaks including limiting visitors, vaccination of staff, furloughing non-critical staff, and screening and exclusion for illnesses consistent with influenza.

e) Unresolved issues

Should this policy also be implemented in prisons or other settings where explosive spread of illness may occur but the risk for severe complications is not high?

7. Healthcare workers in ER, ICU, EMS, and dialysis settings

a) Definition

Includes all staff in these settings who are required for effective functioning of these health care units.

b) Strategy

Prophylaxis

c) Rationale

Optimally effective functioning of these units is particularly critical to reducing the health impacts of a pandemic. Prophylaxis will minimize absenteeism in these critical settings.

d) Population size

Need to obtain population estimates.

e) Unresolved issues

Population sizes

8. Pandemic societal responders and healthcare workers who have no direct patient contact

a) Definition

This group includes persons who provide services that must be sustained at a sufficient level during a pandemic to maintain public well-being, health, and safety. Included are workers at healthcare facilities who have no direct patient contact but are important for the operation of those facilities; utility (electricity, gas, water), waste management, mortuary, and some transport workers.

b) Strategy

Treatment within 48 hours of symptom onset.

c) Rationale

Maintaining certain key functions is important to preserve life and decrease societal disruption. Heat, clean water, waste disposal, and corpse management all contribute to public health. Ensuring functional transportation systems also protects health by making it possible for people to access medical care and by transporting food and other essential goods to where they are needed.

d) Population size

Within these broad categories, there are about 2 million workers at healthcare facilities who have no direct patient contact; 730,000 utility workers; 320,000 waste management workers; 62,000 in mortuary services; and 2.3 million in transportation. Not all occupations within these categories would be classified as pandemic societal responders. Estimates are that 35% of this population will develop illness and present within 48 hours of onset regardless of pandemic severity.

e) Unresolved issues

Need to stratify within these groups to identify who fills specific pandemic societal response functions and to assess whether those functions could still operate if a substantial proportion of the workforce became ill during a 6-8 week pandemic outbreak within a community. Implementation issues need to be addressed, especially with respect to how persons would be identified as falling within this priority group when presenting for treatment and where that treatment would be provided.

9. Other outpatients

a) Definition

Includes persons not in one of the earlier priority groups.

b) Strategy

Treatment within 48 hours of illness onset.

c) Rationale

Treatment reduces the risk of complications and mortality, reduces duration of illness and shortens time off work, and decreases viral shedding and transmission. If sufficient antiviral supplies are available, providing treatment to all who are ill achieves equity and will be most acceptable to the public.

d) Population size

There are an estimated 180 million persons who are not included in previously targeted groups.

e) Unresolved issues

Consider whether there are any strata that can be defined within this population.

C. Additional NVAC recommendations on antiviral drugs for pandemic influenza

In addition to recommendations for priority groups, NVAC unanimously adopted the following recommendations:

- Sufficient drugs should be stockpiled to address top priorities. NVAC recommends that the minimum stockpile size be about 40 million courses, allowing coverage of the top 7 priority groups.
- Oseltamivir should be the primary drug stockpiled, but some zanamivir also should be obtained as it is effective against some oseltamivir-resistant strains, may be preferred for treatment of pregnant women, and supporting two manufacturers enhances security against supply disruptions. Approximately 10% of the stockpile should be zanamivir if feasible and cost effective. No additional adamantanes should be stockpiled.
- Antiviral drugs can also be used as part of an international effort to contain an initial outbreak and prevent a pandemic. Use to slow disease spread early in a pandemic may be useful but requires large amounts of drug.
- Critical research should be conducted to support development and implementation of recommendations for pandemic influenza antiviral drug use, including:
  - Impact of treatment at hospital admission on outcome
  - Optimal treatment dose for H5N1 and other potential pandemic strains
  - Sensitivity and use of rapid diagnostic tests for H5N1 and other influenza strains with pandemic potential
  - Safety and pharmacokinetics of oseltamivir among infants <1 year old
  - Investigation of the impact of other drugs (new antiviral agents and other classes such as statins) on influenza
- Additional work with public and private sector groups should be done to further hone definitions of target groups and their estimated population sizes, and to provide further guidance on antiviral drug distribution and dispensing.

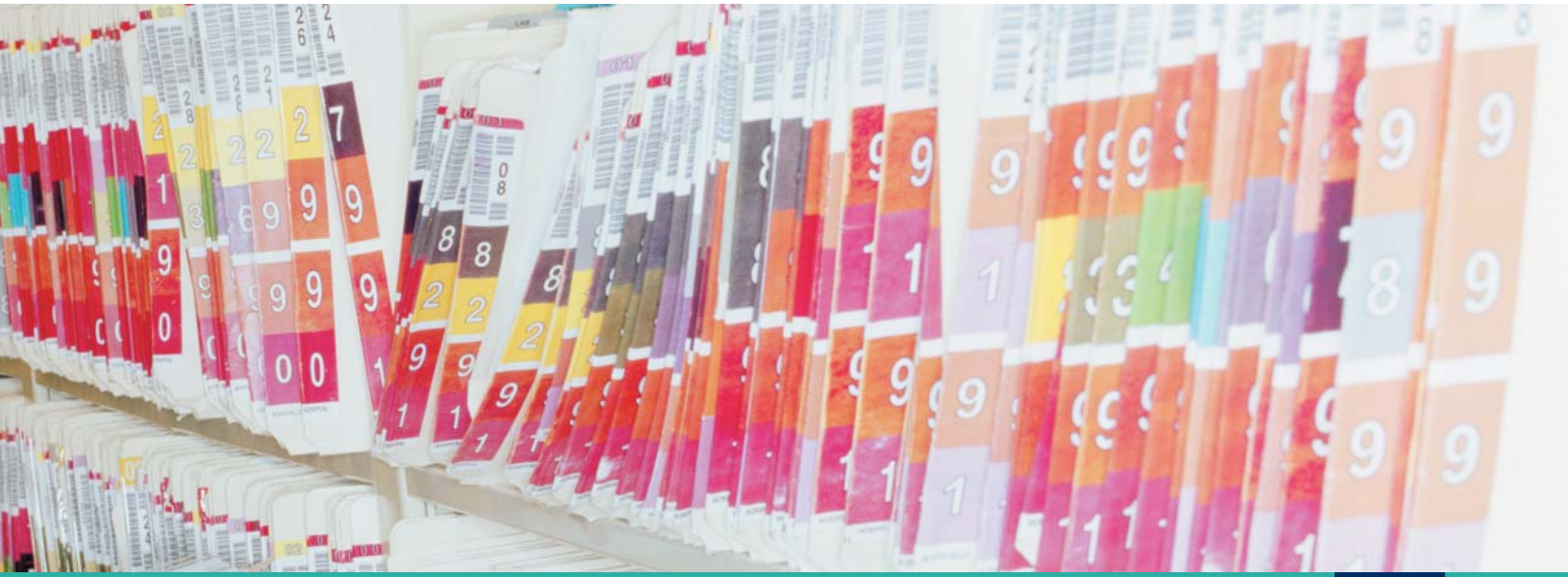
appendix E: legal authorities

Legal authorities

Numerous Federal and state statutes authorize relevant public health actions to address pandemic influenza. Knowledge of these authorities is essential for planning and implementing an effective response to an influenza pandemic.

Section 319(a) of the Public Health Service (PHS) Act (42 U.S.C. 247d), authorizes the HHS Secretary to declare a public health emergency and "take such action as may be appropriate to respond" to that emergency consistent with existing authorities. Appropriate action may include, as otherwise authorized, making grants, providing awards for expenses, entering into contracts, and conducting and supporting investigation into the cause, treatment, or prevention of the disease or disorder that presents the emergency. The Secretary's declaration also can be the first step in authorizing emergency use of unapproved products or approved products for unapproved uses under section 564 of the Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb-3), or waiving certain regulatory requirements of the Department, such as select agents requirements, or—when the President also declares an emergency—waiving certain Medicare, Medicaid, and State Children's Health Insurance Program (SCHIP) provisions. Under the Robert T. Stafford Disaster Relief and Emergency Assistance Act (42 U.S.C. 5121 et seq.), the Federal Emergency Management Agency (FEMA), Department of Homeland Security, is authorized to coordinate the activities of Federal agencies in response to a Presidential declaration of a major disaster or emergency, with HHS having the lead for health and medical services. The President may also declare an emergency under the National Emergencies Act (50 U.S.C. 1601 et seq.)

The PHS Act provides additional authorities for core activities of HHS that will be needed to plan and implement an emergency response. For example, Sections 301, 319F-1, 402, and 405 of the PHS Act authorize the HHS Secretary to conduct and support research. Section 351 of the PHS Act and provisions of the Federal Food, Drug, and Cosmetics Act authorize the Secretary and the FDA to regulate vaccine development and production. Infrastructure support for preventive health services such as immunization activities, including vaccine purchase assistance, is provided under section 317 of the PHS Act. Section 319F-2 of the PHS Act authorizes the Secretary, in coordination with the Secretary of Homeland Security, to maintain the Strategic National Stockpile.



Section 361 authorizes the Secretary to make and enforce regulations necessary to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the United States, or from one state or possession into any other State or possession. CDC administers these regulations as they relate to quarantine of humans. Diseases for which individuals may be quarantined are specified by Executive Order; the most recent change to the list of quarantinable diseases was the April 1, 2005 Executive Order 13375, which amended the Executive Order 13295 by adding "influenza caused by novel or reemergent influenza viruses that are causing, or have the potential to cause, a pandemic" to the list. Other provisions in Title III of the PHS Act permit HHS to establish quarantine stations, provide care and treatment for persons under quarantine, and provide for quarantine enforcement. Section 311 of the PHS Act provides for Federal-state cooperative activities to enforce quarantine and plan and carry out public health activities. Section 311 also authorizes the Secretary to make available the resources of the PHS to help control epidemics and deal with other public health emergencies. HHS may also engage in certain international activities under section 307 of the PHS Act. Statute 42 U.S.C. § 97, which provides that the Secretary of Health and Human Services may request that Customs, Coast Guard, and military officers aid in the execution of quarantines imposed by states. The Secretary also has the authority to implement disease control measures in Indian country, if necessary. (25 U.S.C. 198, 231; 42 U.S.C. 2001). Indian Tribes, like states, are sovereign entities with police power authority to enact their own disease control rules and regulations. Tribal law should be consulted as well.

Further, HHS has broad authority to coordinate vaccine development, distribution, and use activities under section 2102 of the PHS Act, describing the functions of the National Vaccine Program. The Secretary has authority for health information and promotion activities under Title XVII and other sections of the PHS Act. HHS can provide support to states and localities for emergency health planning under Title III of the PHS Act.

Both Federal and state statutes may apply to specific interventions that would be implemented to control a pandemic. Key issues and relevant Federal authority are shown in Table E-1. States should review their authorities to respond to a public health emergency and to take necessary actions for its control.

Table E–1. Key Pandemic Response Components and Legal Authorities.

Issue	Authority
■ Public sector vaccine or antiviral drug purchase	■ Antivirals have been added to the Strategic National Stockpile. ■ At the time of a pandemic, the Federal Government could consider purchasing vaccine or antiviral drugs, if available.
■ Indemnification of manufacturers	■ Executive Order 10789, as amended by Executive Order 13232, extends authorities under P.L. 85-804 to HHS to use indemnification provisions of the Federal Acquisition Regulations, 48 C.F.R. 50.403, if the contractor performs an activity that involves unusually hazardous risks and insurance is not available or sufficient to cover those risks. A contracting officer must review a request for indemnification, and the Secretary must personally approve the request and in some cases consult with Department of Homeland Security and the Office of Management and Budget. ■ Other relevant, but more limited, indemnification authorities such as section 301(a)(7) of the PHS Act may also be available.

Table E–1. Continued

Issue	Authority
■ Distribution of vaccines or antiviral drugs and liability protections	■ The Federal Government may mobilize the PHS Commissioned Corps to distribute vaccines or medications to Federal agencies with direct patient care responsibilities, or to states, tribes, and other localities through the National Disaster Medical System and through agreements between the Federal government, states, and localities. Provision of the medication by particular health care providers is a matter of state law. ■ If a Federal employee administers an antiviral medication or vaccine in the course of his/her official duties, the employee is covered under section 224 of the PHS Act, which makes the Federal Tort Claims Act the exclusive remedy. ■ If the provider were a Federal contractor generally, the contractor would be expected to carry malpractice insurance; expenses of purchasing such insurance generally are an allowable cost of the contract. ■ State employees may be covered for malpractice or tort claims coverage under state law. States should consult their laws on this matter. ■ Private sector employees would generally carry private malpractice insurance. They may also be covered by the Volunteer Protection Act, State Good Samaritan Act, or State Emergency compact provisions.
■ Compensation for persons injured by vaccine or antiviral medications	■ If a person is injured following administration of a vaccine or antiviral medication, in connection with his/her employment, compensation may be available under a state's worker's compensation program. For Federal employees, compensation may be available under the Federal Employees' Compensation Act.
■ Measures to decrease the transmission of infection	■ Individuals may be denied admission to the U.S. if thought to have a communicable disease of public health significance, as defined in CDC regulations. Individuals also may be isolated or quarantined by the Federal Government, or restricted from moving within or between states, if thought to have been exposed to or to be a source of infections to others of a communicable disease listed in an executive order signed by the President. ■ State governors generally may restrict travel within their states and access to their states. Individual state law should be consulted to determine permissible exercise of this authority. ■ States also may impose quarantine. The Secretary may aid states and localities in enforcement of their quarantine actions and accept state and local assistance in enforcing Federal quarantine. ■ In settings such as long-term care facilities where there are public health risks associated with spread of a pandemic strain, states also may be able to compel an individual to take antiviral prophylaxis or be vaccinated, as circumstances warrant. State law should be consulted.

appendix F: current HHS activities

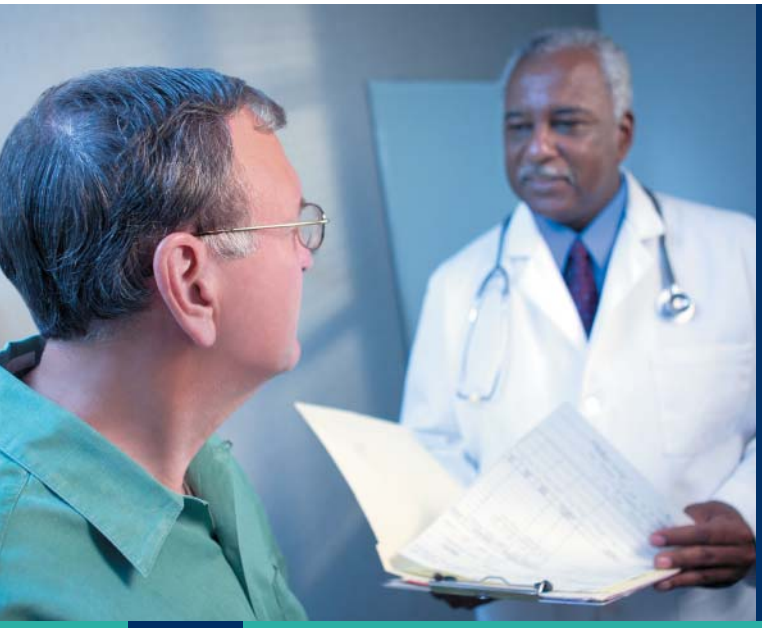
HHS is engaged in a broad array of activities to prepare for an influenza pandemic, although substantial work remains to be done to achieve the capabilities projected in this plan. Ongoing preparedness activities are summarized below.

Planning and Coordination

State and local planning. During the past several years, HHS has provided financial assistance to states to enhance their emergency preparedness activities, including pandemic influenza, through cooperative agreements. CDC provides preparedness funding annually to the public health departments of all the states, certain major metropolitan areas, and other eligible entities through cooperative agreements. HRSA, in conjunction with CDC, awards complementary cooperative agreements to provide preparedness funding annually to the same set of awardees for investment primarily in hospitals and other healthcare entities.

Part 2, Public Health Guidance for State and Local Partners, provides HHS' state partners with guidance, in the form of 11 supplements that provide information they can consider in refining and updating their plans concurrent with the release of the HHS Pandemic Influenza Strategic Plan. A major objective will be to achieve interoperability with the federal government plan and thus compliance with the principles and procedures of the National Response Plan. In particular, HHS will encourage states and municipalities to conduct drills and exercises with which to assess their readiness to respond to an influenza pandemic. HHS will assist federal, state, and local decision-makers in understanding the contents of the Plan. HHS will also work with national associations, such as the Association of State and Territorial Health Officials (ASTHO), to assist in determining their roles and responsibilities.

International collaborations. Sustained human-to-human transmission anywhere in the world will be the triggering event to initiate a pandemic response by the U.S. Because we live in a global community, a human outbreak anywhere means risk everywhere. The U.S. will pursue a containment strategy, where feasible, acting in concert with WHO and other nations as appropriate.



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HHS and the Department of State, Agency for International Development (USAID), the Department of Agriculture (USDA), and other agencies are developing a comprehensive international strategy on avian influenza and pandemic influenza. For example, HHS participates in ongoing global influenza surveillance through the CDC's WHO Collaborating Centers for Influenza. During the current pandemic alert, under the leadership of WHO, surveillance activities have been intensified and include strengthening national influenza center laboratories, training public health personnel, providing diagnostic reagents and other material support, and testing novel virus isolates from humans and animals. HHS has also contributed expertise to the WHO's influenza program and to WHO-led investigations of human cases of avian influenza in Asia. WHO has received additional funding by HHS to strengthen its Global Outbreak and Response Network (GOARN) to assist in surveillance and response worldwide and to establish a fund to ensure that laboratory specimens are shipped in a timely way to reference laboratories for further diagnostic work and confirmation.

As the pandemic threat continues, the U.S. will provide ongoing collaboration and assistance as part of the international response. During a pandemic, under the leadership of the HHS Office of Global Health Affairs (OGHA), the HHS Office of Public Health Emergency Preparedness (OPHEP), and the CDC, expertise and assistance will be provided for a coordinated international response. The U.S is strengthening capacities in the currently affected region of East Asia and enhancing the ability of affected and high-risk countries to address the threat posed by H5N1 avian influenza. Currently, a number of bilateral and multilateral projects are underway in Asian countries to strengthen surveillance and laboratory capacity, develop rapid response capability, develop best practices for clinical case management of those infected, and develop vaccine production capability. In addition, the U.S. is working with the WHO to support international risk communication activities.

The newly formed International Partnership on Avian and Pandemic Influenza, announced by President Bush at the United Nations General Assembly on September 14, 2005, was created to improve international surveillance, transparency, timeliness, and response capabilities. Over 200 delegates from 88 countries and nine international organizations attended the first Senior Officials meeting on October 7, 2005. This initiative will strive for complete transparency, rapid response capabilities, and cooperative surveillance, and will facilitate the sharing of epidemiological data and samples among nations and with the World Health Organization (see Appendix H).

Surveillance, Investigation, and Protective Public Health Measures

Surveillance and epidemiological response. Global collaboration, facilitated by the WHO Secretariat, is a key feature of influenza surveillance. The WHO established an international laboratory-based surveillance network for influenza in 1948, which currently consists of 112 National Influenza Center (NIC) laboratories in 83 countries, and 4 WHO Collaborating Centers for Reference and Research of Influenza (one is located at CDC). The primary purpose of this surveillance network is to detect the emergence and spread of new antigenic variants of influenza, use this information to update the formulation of influenza vaccine, and provide as much warning as possible about the next pandemic. This system provides the foundation of worldwide influenza prevention and control.

The WHO Collaborating Center located at CDC annually produces and distributes worldwide the WHO influenza reagent kits needed to identify the influenza viruses that are expected to circulate. This center also conducts comparative serologic and molecular studies of representative and unusual influenza viruses sent from NIC laboratories around the world.

The newly formed International Partnership on Avian and Pandemic Influenza, announced by President Bush at the United Nations General Assembly on September 14, 2005, was created to improve international surveillance, transparency, timeliness, and response capabilities.

The current HHS surveillance strategy expands the geographic coverage of sentinel disease reporting sites and seeks to improve the timeliness of reporting to public health officials. Clinical and epidemiological assessment tools and investigation strategies are being developed to help guide treatment and assess risk, respectively. Finally, HHS is working to ensure real-time outbreak identification for both domestic and international events. (More information is available at www.cdc.gov/mmwr/preview/mmwrhtml/su5301a13.htm).

Diagnostics and detection. Diagnostic testing for pandemic influenza virus may involve a range of laboratory assays, including rapid antigen tests, reverse-transcription polymerase chain reaction (RT-PCR), virus isolation, and immunofluorescence antibody (IFA) assays. Currently available rapid antigen detection tests are not sufficiently sensitive to reliably distinguish influenza subtypes. In addition, capacity for molecular detection of H5N1, and other strains with pandemic potential, is available at CDC and state reference labs, but is not widely distributed. Capability for production, validation, and distribution of reagents for inclusion in WHO reference typing kits is severely limited.

HHS has augmented state and local laboratory capacity to respond to anticipated surges in laboratory needs by establishing the Laboratory Response Network (LRN). The LRN has trained laboratory personnel in the detection and characterization of novel influenza strains and will work with health departments to provide surge capacity processing and test clinical specimens from patients who meet the case definition of pandemic influenza. Health departments and LRN laboratories will also provide guidelines to clinical laboratories for the safe handling, processing, and testing of specimens. Local public health departments with laboratories not part of LRN or clinical laboratories should contact their state health department for more information regarding laboratory guidelines.

Infection control. On its website, CDC provides guidance to healthcare and public health partners on infection control measures designed to limit the spread of pandemic influenza. Guidance is included on the selection and use of personal protective equipment, such as masks, gloves, and gowns; hand hygiene and safe work practices; cleaning and disinfection of environmental surfaces; handling of laboratory specimens; and post-mortem care. The guidance also covers infection control practices related to the management of infectious patients, the protection of persons at high risk for severe influenza or its complications, personal protection in homes and in communities, and issues concerning occupational health.

CDC recommendations also outline actions that may be taken during the earliest stage of a pandemic when the first potential cases or disease clusters are detected. In this setting, individual-level containment measures (e.g., patient isolation and identification, monitoring, quarantine of contacts) may be useful in slowing the spread of pandemic influenza.

The overall HHS strategy includes a comprehensive approach to protect travelers and decrease entry of pandemic influenza into the United States. This includes: 1) issuing travel advisories and providing education to travelers to decrease their risk of acquiring pandemic influenza infection; 2) identifying persons with influenza-like illness during transit and implementing protocols to limit potential transmission to other passengers; 3) implementing point-of-entry interventions to rapidly identify persons who may have pandemic influenza; 4) isolating persons and identifying and quarantining contacts using fixed quarantine stations and other sheltering models; and 5) attempting to prevent exportation of illness from the United States to other countries and encouraging affected countries to implement similar exit screening.

HHS public health research priorities include evaluating the extent to which infection control measures, such as social distancing, mask use, and hand hygiene, prevent or minimize the spread of pandemic influenza within healthcare settings. Related to these priorities, the study of the relative clinical importance of the various modes of transmission is necessary to better define scientific rationale for various types of personal protective equipment.

Vaccines and Antivirals

Influenza vaccine. Currently, influenza vaccine for the annual, seasonal influenza program comes from four manufacturers. However, only a single manufacturer produces the annual vaccine entirely within the U.S. Thus, if a pandemic occurred and existing U.S.-based influenza vaccine manufacturing capacity was completely diverted to producing a pandemic vaccine, supply would be severely limited. Moreover, because the annual influenza manufacturing process takes place during most of the year, the time and capacity to produce vaccine against potential pandemic viruses for a stockpile, while continuing annual influenza vaccine production, is limited. Since supply will be limited, it is critical for HHS to be able to direct vaccine distribution in accordance with predefined groups (see Appendix D); HHS will ensure the building of capacity and will engage states in a discussion about the purchase and distribution of pandemic influenza vaccine.

Vaccine production capacity: The protective immune response generated by current influenza vaccines is largely based on viral hemagglutinin (HA) and neuraminidase (NA) antigens in the vaccine. As a consequence, the basis of influenza vaccine manufacturing is growing massive quantities of virus in order to have sufficient amounts of these protein antigens to stimulate immune responses. Influenza vaccines used in the United States and

The overall HHS strategy includes a comprehensive approach to protect travelers and decrease entry of pandemic influenza into the United States.

HHS is currently supporting a number of vaccine manufacturers in the advanced development of cell-based influenza vaccines with the goal of developing U.S.-licensed cell-based influenza vaccines produced in the United States.

around world are manufactured by growing virus in fertilized hen's eggs, a commercial process that has been in place for decades. To achieve current vaccine production targets millions of 11-day old fertilized eggs must be available every day of production.

In the near term, further expansion of these systems will provide additional capacity for the U.S.-based production of both seasonal and pandemic vaccines, however, the surge capacity that will be needed for a pandemic response cannot be met by egg-based vaccine production alone, as it is impractical to develop a system that depends hundreds of millions of 11-day old specialized eggs on a standby basis. In addition, because a pandemic could result from an avian influenza strain that is lethal to chickens, it is impossible to ensure that eggs will be available to produce vaccine when needed.

In contrast, cell culture manufacturing technology can be applied to influenza vaccines as they are with most viral vaccines (e.g., polio vaccine, measles-mumps-rubella vaccine, chickenpox vaccine). In this system, viruses are grown in closed systems such as bioreactors containing large number of cells in growth media rather than eggs. The surge capacity afforded by cell-based technology in insensitive to seasons and cane be adjusted to vaccine demand, as capacity can be increased or decreased by the number of bioreactors or the volume used within a bioreactor. In addition to supporting basic research on cell-based influenza vaccine development, HHS is currently supporting a number of vaccine manufacturers in the advanced development of cell-based influenza vaccines with the goal of developing U.S.-licensed cell-based influenza vaccines produced in the United States.

Dose-sparing technologies. Current U.S.-licensed vaccines stimulate an immune response based on the quantity of HA (hemagglutinin) antigen included in the dose. Methods to stimulate a strong immune response using less HA antigen are being studied in H5N1 and H9N2 vaccine trials. These include changing the mode of delivery from intramuscular to intradermal and the addition of immune-enhancing adjuvant to the vaccine formulation. Additionally, HHS is soliciting contract proposals from manufacturers of vaccines, adjuvants, and medical devices for the development and licensure of influenza vaccines that will provide dose-sparing alternative strategies.

Antiviral drugs. One of currently circulating H5N1 virus strains is resistant to one of two existing classes of antiviral drugs. Only the neuraminidase inhibitors, oseltamivir (Tamiflu®) and zanamivir (Relenza®) provide clinical benefit against all of the H5N1 virus strains currently circulating in Asia. As of October 2005, the Strategic National Stockpile includes 2.3 million treatment courses of oseltamivir (Tamiflu®) and 84,000 treatment courses of zanamivir (Relenza®). The Strategic National Stockpile is expecting delivery on an additional 2 million courses of Tamiflu by the end of 2005. HHS is committed to acquiring additional courses of these drugs, as stated earlier, and increasing U.S.-based antiviral production.

Further research and development. HHS plans to accelerate basic discovery in priority areas such as natural history of influenza progression, animal-to-human transmission of disease, and virus/host interaction. It plans to do this by supporting academic and private-sector research grants in priority areas that could contribute to the generation of new vaccines, drugs, and diagnostics and expanding support for multidisciplinary focus in priority areas.

HHS also plans to accelerate development of vaccines, drugs, and diagnostics by 1) supporting and accelerating the clinical testing of candidate products that are in advanced states of development (e.g. recombinant influenza vaccine and new and/or long-acting neuraminidase inhibitor antiviral drugs); 2) supporting evaluation and licensure efforts for injectable and pediatric formulations of currently licensed drugs, of new antiviral drugs, 3) supporting accelerated preclinical development including in vitro and animal model studies of promising countermeasures (e.g. siRNA and common-epitope vaccines, new immune-stimulating adjuvants, novel antiviral drugs, and genomic/proteomic microchip approaches to rapid diagnostics using surrogate markers of early infection). These will be accomplished using milestone-driven grants with private-sector partners and public/private sector collaborations; 4) supporting revised protocols and increased resources to reduce the time to prepare and qualify influenza virus reference strains used in vaccine manufacturing and to calibrate HA content in influenza vaccines for potency assays; and 5) developing accurate, rapid point-of-care diagnostic tests for clinical use during a pandemic, which will require additional investment in new technology leading both to better diagnosis of influenza and differentiation among the various respiratory infections.

Healthcare and Emergency Response

Clinical care. HHS is working with the medical community to establish clinical procedures for the initial screening, assessment, and management of patients with suspected novel influenza during a pandemic. Early recognition of illness caused by a novel influenza virus strain will rely on a combination of clinical and epidemiological features. Guidelines for the management of influenza-related complications, including community-acquired pneumonia, have also been developed.

Healthcare surge capacity. An influenza pandemic may increase the demand for hospital inpatient and intensive care unit (ICU) beds and assisted ventilation services by more than 25%. HHS is developing a deployable mass casualty capability that could be used to supplement hospitals. HHS recommends that hospitals develop their own response plans. **Supplement 3** provides guidance to hospitals on several components of a plan including hospital surveillance, hospital communication, staff education and training, triage and admission procedures, staffing and bed capacity, consumable and durable supplies, and planning for provision of care in non-hospital settings.

Psychosocial support services. HHS is focusing on the institutionalization of psychosocial support services that will help healthcare workers manage emotional stress during the response to an influenza pandemic and resolve related personal, professional, and family issues. HHS is also addressing the preparation of informational materials for employees and their families and the development of workforce resilience programs to assist families of deployed workers.

Mass fatalities and mortuary services. HHS understands that the timely, safe, and respectful disposition of the deceased is an essential component of an effective response. Pandemic influenza may quickly rise to the level of a catastrophic incident that results in mass fatalities, which will place extraordinary demands (including religious, cultural, and emotional burdens) on local jurisdictions and the families of the victims. A catastrophic incident involving mass fatalities will require federal assistance to transport, process, and store deceased victims and support final disposition and personal effects processing. Most local jurisdictions will be severely strained to handle mass fatalities or may experience profound difficulties.

If local and state fatality management capacities are exceeded, HHS, under ESF #8, will coordinate with the Department of Homeland Security (DHS) and the Department of Defense (DoD) to assist in providing mortuary services; establishing temporary morgue facilities; and processing, preparation, and disposition of human remains.

An influenza pandemic may increase the demand for hospital inpatient and intensive care unit (ICU) beds and assisted ventilation services by more than 25%. HHS is developing a deployable mass casualty capability that could be used to supplement hospitals.

Communications and Outreach

Risk communication. HHS is the federal government's lead agency in pandemic influenza communications. An HHS Communications and Public Outreach Strategy for Pandemic Influenza has been developed. This strategy is designed to prepare U.S. citizens and communities for a pandemic; communicate the need for local preparedness and an understanding of the implications of a pandemic; and develop consistent, clear, honest messages and materials that can be shared broadly in the U.S. and with global partners. Components of the strategy include 1) assessment of current public (or community) knowledge through ongoing surveillance of media and surveys of the public and providers; 2) development of materials such as message maps that have been developed and tested in focus groups; 3) formative audience research; 4) cross-government communication coordination; 5) facilitating community and business continuity planning by helping these sectors communicate with their constituents and prepare; 6) public engagement through forums and stakeholder meetings on such important policy issues as allocation of limited drugs and vaccines; 7) web communications development through a consolidated, centralized U.S. government website; 8) international outreach to support our global partners, in cooperation with the WHO Secretariat; and 9) continuing efforts to raise awareness about the importance of seasonal influenza vaccine and to promote increased yearly compliance of influenza and pneumococcal vaccination.

A Public Engagement Pilot Project on Pandemic Influenza was initiated in July 2005 to discuss goals for a pandemic influenza vaccination program and to pilot test a new model for engaging citizens on vaccine related policy decisions. The pilot project was sponsored by interested organizations including the Atlanta Journal Constitution, the Lounsbery Foundation, the Keystone Center, the Institute of Medicine, the University of Georgia, the CDC's National Immunization Program, the HHS National Vaccine Program Office, and the Study Circles Resource Center. To conduct this public consultation, the sponsors made use of an innovative model for engaging stakeholders from various organizations with an interest in pandemic influenza, and individual citizens-at-large from the 4 principal regions of the United States. The anticipated major benefits from this public consultation were the development of an improved plan to combat pandemic influenza and one more likely to gain public support, and a demonstration that citizens can be productively engaged in informing vaccine-related policy decisions. A complete assessment of the potential benefits from this pilot project is still underway and important potential outcomes such as improved relationships and increased trust among the participants have not been yet been measured.

HHS understands that the timely, safe, and respectful disposition of the deceased is an essential component of an effective response.

appendix G

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I. INTRODUCTION

Influenza is not a disease that can be eradicated. Wild birds and domestic animals harbor influenza A viruses, which have the potential for direct transmission to man and for genetic recombination with human influenza A strains. As a result, animal reservoirs present opportunities for the emergence of influenza A viruses that are antigenically novel to the human immune system. The emergence of such a virus that develops the ability for person-to-person transmission could lead to an influenza pandemic. Although exactly when and where the next influenza pandemic will occur is unknown, it is possible that the outcome will vary from serious to catastrophic. Expanding research on influenza before the next pandemic occurs will promote a better understanding of influenza and will lead to new strategies and products that could improve the effectiveness of a pandemic response and prevent disease and death.

Research on influenza is conducted by several HHS and other U.S. government agencies such as the Department of Defense, Department of Veteran's Affairs, and the Department of Agriculture. The largest proportion of influenza research is supported by the National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), primarily through investigator-initiated grants and contracts. These agreements support both basic and applied research on influenza virus biology, epidemiology, pathogenesis, and immunology, as well as the development of new and improved influenza diagnostics, antiviral drugs, and vaccines. Other influenza research is supported through the intramural program at NIH, including the Laboratory of Infectious Diseases (LID), which also has a strong focus in new vaccine development.

The Centers for Disease Control and Prevention (CDC), through the National Center for Infectious Diseases and the National Immunization Program, supports a broad intramural and collaborative influenza research portfolio including studies on influenza epidemiology, immunology, vaccines, and vaccination programs.

The Food and Drug Administration's (FDA) Center for Biologics Evaluation and Research (CBER) and Center for Drug Evaluation and Research (CDER), conduct and/or advise on research on influenza vaccines and antivirals, respectively.

The Agency for Healthcare Research and Quality (AHRQ) supports research on surge capacity, the use of information systems for bed-tracking and syndromic surveillance in emergency departments, and primary care.

Expanding research on influenza before the next pandemic occurs will promote a better understanding of influenza and will lead to new strategies and products that could improve the effectiveness of a pandemic response and prevent disease and death.

The intent of the NRP is to reduce America's vulnerability to terrorism, major disasters, and other emergencies; to minimize the damage resulting from these emergencies; and to facilitate recovery.

In April 2005, the Institute of Medicine (IOM) convened The John R LaMontagne Memorial Symposium on Pandemic Influenza Research to address the current state of the research and outline future priorities of scientific research for pandemic influenza. HHS will consider these recommendations, as well as other outside expert opinion, as the basis for scientific research in influenza in the near future. The combined efforts of HHS agencies including NIH, CDC, and FDA, as well as the private sector, will be needed to develop and implement this research agenda.

Research has provided the underpinning of many of the tools HHS currently has to combat influenza and will be the basis of those that are developed in the future. This document will summarize critical HHS influenza research activities. As much of the research on influenza A is applicable to both interpandemic (H3N2 & H1N1) and pandemic influenza, this document will cover both.

A. Critical basic research foundation

Basic research on influenza facilitates new ways of detecting and rapidly characterizing these viruses as they emerge. Most Federal funds currently available for influenza research are provided through NIH in the form of grant support for scientists to study fundamental issues related to basic biology, virology, immunology, pathogenesis, and the development of new diagnostics, antiviral agents, and vaccines. In addition, NIAID supports centralized research resources such as contracts to screen new drugs, develop new animal models, and establish a reagent repository. These resources are available to research scientists around the world and contribute to pandemic preparedness.

Basic research on the virus and its structure, the factors that contribute to its virulence, and its ability to evade the immune system, and an understanding of the genetic changes that permit an influenza virus to suddenly acquire the ability to transmit between species, provide important information for fighting pandemic influenza. The development of new systems for manipulating influenza genes to create strains (referred to as "reverse genetics") provides researchers with the opportunity to systematically uncover the function and interactions of each gene in the influenza virus genome. The application of this technology has already begun to expand understanding of virus-host range restriction, viral replication, and pathogenicity in order to speed the production of inactivated and live-viral vaccine candidates.

Through NIH and private sector-supported applied research programs, new vaccine candidates are being developed and clinically tested.

An increasing number of materials and reagents are being made available through the NIAID Influenza Reference Repository, the CDC WHO Collaborating Center, and FDA/CBER, including antibodies and reference antigens to a number of avian influenza viruses considered to be of high pandemic potential. Updating the reagents in this library and making them available to research scientists around the world remains an area of high priority.

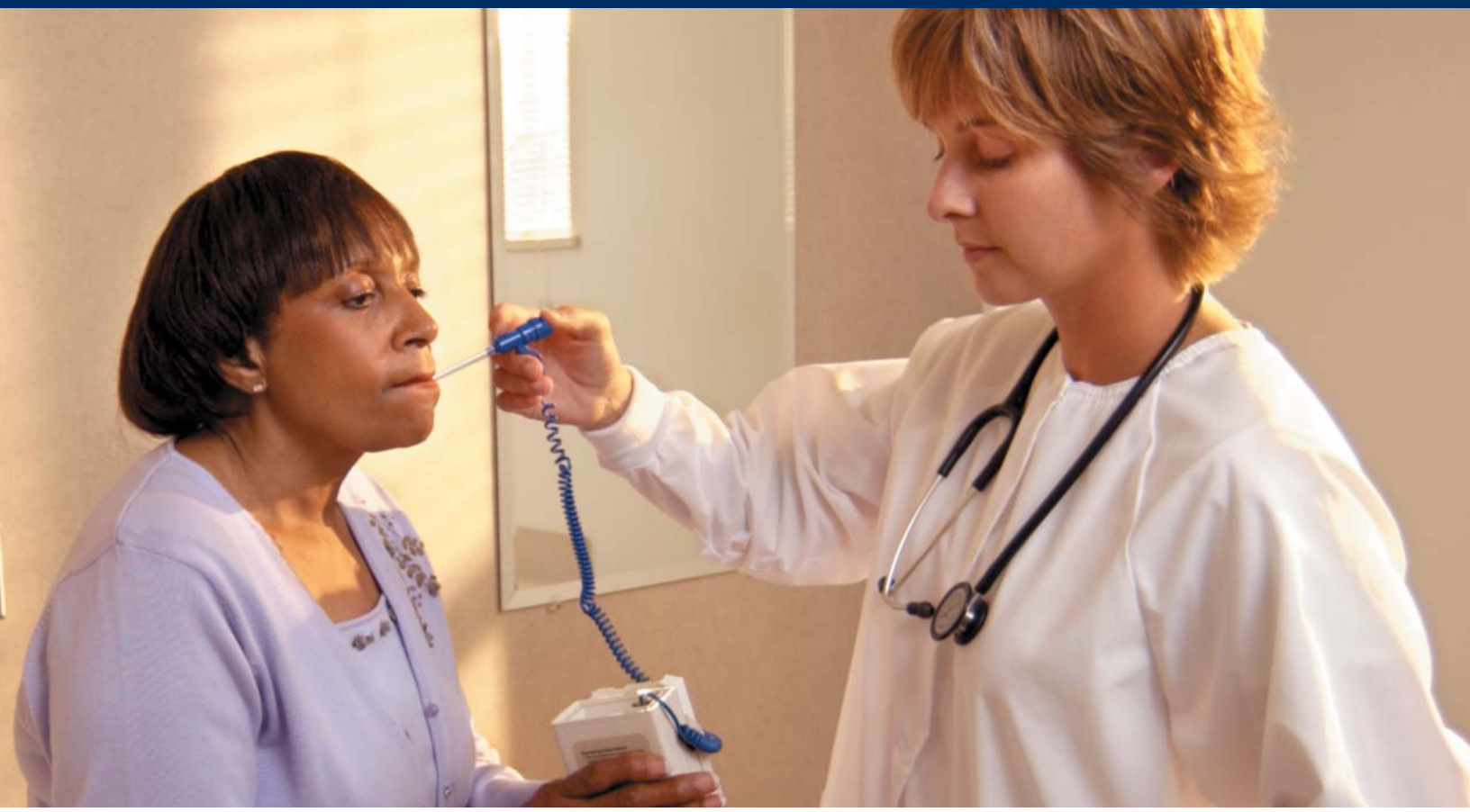
B. The transition to applied research

The plasticity of the influenza genome facilitates the virus's adaptability and its ability to escape the specific host immune responses, leading to the need for annual vaccination with updated vaccine. Through NIH and private sector-supported applied research programs, new vaccine candidates are being developed and clinically tested. One successful public-private partnership has been the government's long-standing involvement in the development of the live-attenuated influenza virus vaccine, which was licensed by the FDA in 2003.

Efforts are also underway to enhance the immunogenicity of inactivated influenza vaccines (especially for very young and very old individuals) by administering them using new delivery systems, providing them in higher doses, or by combining them with adjuvants or supplemental proteins. Vaccines that contain common protein epitopes from influenza viruses may provide generic protection against a wide range of influenza viruses and are being aggressively pursued. While the exact subtype of influenza virus that will cause the next pandemic is not known, producing prototypic vaccine reference strains that can be used in developing vaccine candidates is essential for preparedness and is being supported by the CDC, FDA, the NIH, and other international laboratories. Production and clinical testing of investigational lots of vaccines made with these reference strains should be supported as they become available.

In addition to vaccine-related research, the NIH supports several programs on the development of new antiviral agents against influenza. These programs range from target identification to the support of clinical trials. In vivo and in vitro screening programs to identify promising drug candidates provided by private sector companies and academic laboratories are also ongoing.

The NIAID Biodefense Partnership and Challenge Grant Programs provide support to private sector companies to develop new vaccines against influenza, including non-egg based vaccine platforms, new antiviral drugs against influenza, and genomics-based diagnostic assays against a number of acute respiratory viruses, including influenza.



Applied research also leads to the development of tools and to refinement of strategies that are critical to effective surveillance and pandemic response programs. Improved influenza rapid diagnostic tests, development of more sensitive and rapid laboratory assays for detecting and subtyping influenza viruses, and new high capacity methods to test influenza virus strains for susceptibility to antiviral drugs—and their implementation at CDC, public health, and hospital laboratories—all are key to identifying and tracking disease before and during a pandemic, and to providing public health and health care providers the information needed to make optimal decisions.

Another component of applied research relates to the AHRQ support for research on health system preparedness. This work has focused on the use of real-time information systems to track hospital bed capacity, including emergency department and ventilator beds. In addition, a mass prophylaxis and vaccination program is currently part of the Cities' Readiness Initiative and the Strategic National Stockpile training activities.

In addition, epidemiological, programmatic, and behavioral research results lead to new understanding of influenza infections including their consequences and who is at risk, strategies to improve vaccination delivery and help eliminate racial and ethnic disparities, and effective communications messages and tools that will be vital to a pandemic response.

This appendix identifies ongoing HHS research activities for influenza, as well as highlights future research priorities that will allow the U.S. to prepare, respond, and reduce the overall morbidity and mortality associated with pandemic influenza.

II. U.S. PANDEMIC INFLUENZA: RESEARCH ACTIVITIES AND NEEDS

A. Basic virology and molecular biology

Influenza viruses, members of the family Orthomyxoviridae, are classified into three types: A, B, and C, with influenza A causing the most severe disease in humans and the most likely to trigger a pandemic. While a number of structural proteins have been identified in influenza A viruses, the two surface proteins, the hemagglutinin (HA) and neuraminidase (NA), play key roles in the pathogenesis of the virus and the host's immune response. Although only two influenza A subtypes currently co-circulate globally in humans (H1N1 and H3N2), at least 16 distinct antigenic subtypes of HAs (H1 to H16) and nine NAs (N1 to N9) have been identified in wild aquatic birds. In spite of the severity of influenza disease, little is known about the role of the viral proteins in the virus' pathogenicity or transmission.

Goals:

- Understand the mechanism(s) by which influenza viruses of any novel subtype emerge in humans and animals.
- Identify genetic mutations that correlate with antiviral resistance.

Ongoing HHS activities:

- Conducting studies to examine the molecular biology and epidemiology of pathogenic viruses in avian reservoirs, with a focus on defining the molecular basis of virulence for avian viruses such as the 1997 and 2004–2005 H5N1 viruses and the role of virulence factors and pathogenic determinants in disease
- Using the Influenza Genome Sequencing Project to put influenza sequence data rapidly in the hands of scientists, enabling them to further study how influenza viruses evolve, spread, and cause disease
- Establishing libraries of antigenically and genetically characterized human and animal influenza viruses
- Developing new rapid methods to detect antiviral resistance in clinical influenza isolates
- Studying viral evasion mechanisms to the innate immune response mechanism, and how influenza A and B viruses modulate the innate defenses of the host
- Examining the molecular basis of transmission of influenza viruses among animals and humans

Future priorities:

- Determine the compatibility of gene segments derived from human and animal influenza viruses to reassort—an event that may result in the emergence and interspecies transmission of novel influenza viruses.
- Evaluate the role of mutations and constellations of mutations in antiviral drug resistance using a reverse genetics system to find viruses with specific mutations associated with drug resistant phenotypes.
- Examine the reason behind the high lethality of the 1918 influenza pandemic.
- Identify the pandemic influenza genes that have the greatest potential for interspecies transfer. Research the role of other viral proteins in the pathogenesis of influenza.

- Identify and characterize the intracellular trafficking of influenza virus proteins, nucleic acids and complexes in avian and mammalian systems.
- Research the structural diversity of sialosides expressed at the surface of airway epithelial cells in avian and mammalian species.
- Conduct comparative analysis of membrane fusion mechanisms by HA in avian and mammalian cells.
- Research interactions between HA and mucins from avian and mammalian airway.
- Optimize reverse genetic techniques to facilitate isolation of reassortant influenza viruses.
- Research the role of other viral proteins in the pathogenesis of influenza.
- Determine the molecular basis of virulence in humans and animals.
- Support studies on the evolution and emergence of influenza viruses, including the identification of factors that affect influenza host-range and virulence.

B. Animal surveillance

Animal surveillance of influenza is important for several reasons. Previous epidemics of human infection with influenza in 1957 and 1968 were preceded by circulation of these viruses in animals. This was likely true in 1918 also, though the specific source is not clear. In addition, outbreaks in animals can be associated with considerable economic costs due to culling of infected animals and reduction in trade.

Recent outbreaks in domestic poultry in Asia associated with cases of human disease highlight the importance of coordinating surveillance activities. Surveillance for influenza A viruses in poultry in the U.S. has increased since the outbreak of highly pathogenic avian influenza (HPAI) in Pennsylvania and surrounding states in 1983 and 1984. Investigations may be conducted by state animal health officials, USDA-accredited veterinarians, university personnel, or members of the poultry industry. Samples from affected flocks are routinely submitted to state laboratories for diagnosis. If importation of HPAI is suspected, a Foreign Animal Disease Diagnostician will conduct an investigation and submit samples directly to the National Veterinary Services Laboratories (NVSL) in Ames, Iowa.

Recent outbreaks in domestic poultry in Asia associated with cases of human disease highlight the importance of coordinating surveillance activities.

Most birds submitted for entry into the United States must be quarantined in USDA-approved quarantine facilities. During quarantine, avian influenza virus isolation is attempted on samples collected from all dead birds and some live birds.

Surveillance in the U.S. for influenza A viruses in swine and horses is currently less systematic than in poultry. While no requirement exists for USDA notification when cases or outbreaks of influenza occur in these animals, considerable interest exists in understanding the viruses that are circulating among them. In general, only outbreaks in swine of unusual severity or duration are likely to be investigated and reported. On the other hand, surveillance for influenza viruses causing disease in horses has practical utility because data generated from analysis of equine influenza viruses can be used to guide equine influenza vaccine formulation.

Goal:

- Understand the prevalence, ecology, and spread of influenza virus subtypes in animal reservoirs.

Ongoing HHS activities:

- Conducting an ongoing animal influenza surveillance program in Hong Kong and other parts of Asia in wild birds, live bird markets, and pigs
- Conducting an annual surveillance of influenza viruses in wild migrating birds in North America and collaborating with the Canadian Wildlife Service to isolate influenza viruses from migratory birds

In addition to the HHS activities, other agencies are also conducting animal research.

- WHO has initiated limited systematic influenza surveillance in swine, and recent avian outbreaks caused by highly pathogenic influenza strains are likely to lead to new avian surveillance activities.
- The Office International des Epizooties (OIE) has established reference laboratories for avian and equine influenza. These laboratories provide diagnostic testing including virus characterization, reagents, and training. The OIE member countries report outbreaks of avian, equine, and swine influenza, and the OIE prepares a yearly summary of these reports.
- The Animal Health Trust, Newmarket, U.K., has taken the lead in organizing a program for equine influenza surveillance and reporting.
- The U.S. Department of Agriculture (USDA) conducts influenza surveillance in domestic animals.
- The USDA's Animal and Plant Health Inspection Service (APHIS) has been monitoring live bird markets in the northeastern region of the U.S. since 1986 for the presence of avian influenza viruses that may pose a threat to commercial poultry.

Future priorities:

- Expand surveillance of influenza viruses in poultry, swine, and wild migratory birds in the U.S. and abroad.
- Sequence known human and animal influenza viruses to understand their molecular evolution.

Year-round influenza surveillance provides information on the baseline level of influenza activity during the summer, and these data have the potential to become an important component of early detection for a pandemic.

C. Human surveillance and epidemiology

The information regarding circulating influenza strains is used to monitor global influenza activity and to update the formulation of annual influenza vaccines. It is also used to detect novel influenza strains (i.e., influenza A subtypes that have not recently circulated among people) that infect humans, leading to the implementation of control measures and providing early warning of a possible pandemic.

CDC conducts and coordinates influenza surveillance in the United States. Surveillance focuses on collecting influenza viral isolates for testing, monitoring morbidity and mortality, and identifying unusual or severe influenza outbreaks (see Part 2, **Supplement 1**). The U.S. national influenza surveillance system includes: laboratory surveillance, outpatient influenza-like illness (ILI) surveillance, pneumonia and influenza (P&I) related mortality surveillance, and an assessment of influenza activity at the state level. Traditionally, U.S. influenza surveillance has been conducted from October through mid-May, but is now being conducted year-round. Year-round influenza surveillance provides information on the baseline level of influenza activity during the summer, and these data have the potential to become an important component of early detection for a pandemic.

Goals:

- Understand the prevalence of disease in select populations or other groups.
- Understand the factors involved in transmission of influenza.
- Understand the efficacy of potential control measures.

Ongoing HHS activities:

- Partnering with the WHO through the Global Outbreak Alert and Response Network (GOARN) to assure overall improvements in global disease detection and control
- Providing additional support and assistance to foreign governments for the development or improvement of influenza surveillance networks
- Providing support for BioSense: a state-of-the-art, multi-jurisdictional, data-sharing program to facilitate surveillance of unusual patterns or clusters of disease activity around the country
- Conducting surveillance of pediatric influenza-associated deaths, using the national reportable disease list by the Council of State and Territorial Epidemiologists, to aid in the identification of high-risk groups and in formulating improved immunization policies

- Conducting surveillance through the New Vaccine Surveillance Network to detect all influenza cases among children <5 years old who are admitted to a hospital to evaluate the effectiveness of influenza vaccination and the costs associated with pediatric influenza illness
- Supporting Emerging Infections Program network sites, which characterize the burden of severe, laboratory-confirmed pediatric influenza in the U.S.
- Supporting the Models of Infectious Disease Agent Study (MIDAS), which develops computational models that are agent-based, taking account of how individual people interact in their daily lives and examining how a pandemic might spread under various approaches to intervention
- Conducting studies to obtain annual estimates of vaccine effectiveness against laboratory- confirmed influenza illness that are underway
- Making interagency agreements with DoD for support of Naval Medical Research Unit [NAMRU] 2 (Jakarta) & 3 (Cairo) for surveillance of influenza and emerging infectious diseases
- Evaluating the role of children as vectors for the transmission of influenza infection within a community and the impact/use of vaccines to reduce spread and potentially alter the course of an epidemic

In addition, the World Health Organization (WHO) supports an international laboratory-based surveillance network for influenza to detect the emergence and spread of new antigenic variants of influenza.

Future priorities:

- Conduct serological studies of humans who are in close contact with animal reservoirs to assess both cross-species transmission and subsequent human-to-human transmission.
- Determine population effects of vaccines by studying the impact of vaccination on annual influenza epidemics, developing models for predicting the impact of annual vaccination on a future pandemic, and establishing the cost savings of different vaccination programs.
- Determine the impact of antiviral drugs and increasing social distance measures in annual influenza epidemics, including studying the evolution of resistance and describing the behavior of individuals during an outbreak.
- Develop further analytical and computational models to study the potential impact of strategies to prevent emergence, contain spread, reduce mortality and morbidity, and make good use of limited resources. Models need to examine the individual and combined impact of intervention strategies.
- Establish a database of influenza subtypes, including sequences, clinical information, and temporal and geographic data.
- Examine the transmission of influenza viruses specifically in healthcare settings, evaluating the use of different personal protective equipment devices to prevent spread and the impact of vaccinating health care workers.

D. Immune response parameters

Historical experience with influenza vaccines suggests that two doses of inactivated vaccine will be needed to induce adequate levels of immunity to a pandemic strain of influenza. Enhancing the immunogenicity of a pandemic vaccine so that a one dose course could be used could ultimately reduce the time and cost required to protect the population. This may require inclusion of an adjuvant—a substance included in vaccines to increase the strength of the immune response—in the formulation of a pandemic vaccine. Further investigation needs to be done to understand whether adjuvants will be useful in a pandemic situation.

Goals:

- Determine how to further enhance the immunogenicity of influenza vaccines through adjuvants or alternative delivery approaches.
- Optimize immunological assays.
- Define serologic correlates of immunity.

Ongoing HHS activities:

- Developing new adjuvants
- Identifying immunologic markers that might correlate to immunity
- Evaluating mechanisms of secondary infections after influenza infections
- Creating "Immune Modeling Centers" that simulate human innate immune responses to adjuvants or immune modulators
- tudying immune responses to influenza vaccination in special populations and defining the immune parameters responsible for vaccine failure/response

Future priorities:

- Defining further the immunological markers (such as cell mediated immunity, cytokine production) that might constitute correlates of protection and determine the role of humoral, cellular, and mucosal immunity in protection against influenza disease, with an emphasis on those populations at highest risk
- Developing serological assays to assess immune responses to help researchers determine the immune mechanisms responsible for strong vs. weak immune responses to influenza vaccines
- Developing and evaluating new adjuvants
- Evaluating established and new immunotherapies on infections caused by novel influenza viruses
- Evaluating innate immune effector molecules (such as surfactants, mannose binding lectins, defensins, etc.) in the treatment of influenza
- Evaluating innate immune activation molecules (TLR 3,4,7,8,9 agonist, NOD receptors, etc.) in the treatment of influenza
- Developing modulators of inflammatory cascades

Early detection of new influenza outbreaks is critical to limit the spread of infection and control its impact on human health.

E. Diagnostic tools development

Early detection of new influenza outbreaks is critical to limit the spread of infection and control its impact on human health. The influenza diagnostic tests that are currently available have limited sensitivity and specificity and are not able to discriminate between viral subtypes. Novel diagnostic tools are needed in the detection of newly emerging influenza strains and to discriminate between different influenza subtypes.

The ability to test new diagnostic technologies in public health laboratory settings is also being enhanced through the distribution of standardized protocols for lab methods by introducing new techniques, such as multiplex PCR, and by expanding the role for use of molecular techniques to rapidly diagnose respiratory agents, including influenza types and subtypes.

Goal:

- To support the development of rapid and reliable diagnostic tests for the identification and characterization of epidemic and pandemic influenza viruses.

Ongoing HHS activities:

- Developing new rapid antigen detection methods
- Developing subtype specific reference antisera for use in the rapid identification of novel influenza viruses
- Standardizing molecular techniques for the identification of influenza virus types and subtypes, including those normally circulating in human populations (H1, H3) and recent avian subtypes of interest (H5, H7 and H9)
- Developing a diagnostic microarray for influenza A (the "Flu Chip") that will provide information as to whether or not an individual is infected with influenza as well as provide both type and antigenic subtype characterization of the virus
- Developing new diagnostics that can discriminate between several different causes of respiratory diseases, including avian influenza and SARS
- Developing techniques for identifying host-response profiles for early pre-symptomatic infections

Future priorities:

- Develop more new technologies and platforms that allow for the detection and discrimination of newly emerging influenza virus subtypes.
- Develop new rapid antigen detection methods for use on clinical specimens obtained from patients infected with a novel influenza.
- Develop new rapid methods to detect antiviral resistance in clinical influenza isolate.
- Develop techniques for identifying host-response profiles for early detection of pre-symptomatic infections.

F. Antiviral drug development

In the event of a pandemic, antiviral drugs will be the first line of defense before a vaccine is available and could delay the spread of the pandemic, particularly if the strain is not efficiently transmitted between humans. There are currently two classes of antiviral drugs against influenza: the neuraminidase inhibitors and the M2-ion channel blockers known as adamantanes. Studies have shown that neuraminidase inhibitors, in addition to being active against influenza A and B, may reduce complications of influenza in some individuals. H5N1 viruses isolated from poultry and humans in Asia in 2004 are known to be resistant to the adamantanes. The development of new anti-influenza drugs with broad activity and diminished risks of resistance emergence is of great importance.

Goals:

- Partner with industry, academia, and other interested parties to develop new influenza antiviral agents that can that can provide an option for therapy and chemoprophylaxis if strains that are resistant to currently available agents emerge and spread.
- Examine various treatment strategies to guide decision-making around the use of limited antiviral supplies.

Ongoing HHS activities:

- Evaluating monotherapy vs. combination therapy in the treatment of novel influenza infections
- Developing novel long-acting neuraminidase inhibitors
- Developing novel therapeutics using inhibitors of fusion proteins that may be capable of blocking infections by all strains of influenza viruses
- Investigating RNA interference of influenza virus infection as a new way of preventing and treating influenza infection
- Supporting "Immune Modeling Centers" which develop computational models to screen novel compounds for future clinical applications against influenza infection
- Supporting a clinical trial infrastructure (e.g., networks of potential sites with appropriate communication, documentation, and collaboration) to evaluate new influenza antiviral drugs

In the event of a pandemic, antiviral drugs will be the first line of defense before a vaccine is available and could delay the spread of the pandemic.

Future priorities:

- Expand preclinical and clinical support for the development of new promising antiviral drugs against influenza.
- Monitor for the emergence of antiviral resistance.
- Conduct studies to improve programmatic feasibility of stockpiling antiviral drugs.
- Conduct clinical trials of potentially resource-sparing approaches such as dose reduction and shortened treatment courses that might contribute to the testing of new public health strategies.
- Develop inhaled antibodies for immunoprophylaxis against influenza.
- Support continued development of other agents with activity against influenza including hemagglutinin inhibitors, polymerase inhibitors, and protease inhibitors.
- Study antiviral drug efficacy in severely ill hospitalized patients (including treatment started late in disease course).
- Study antiviral drug effects on severe influenza complications.
- Evaluate safety and dosing in infants with influenza, and alternative dosing regimens/formulations for infants and young children.
- Establish a pregnancy registry to prospectively collect data on exposures and outcomes.

G. Vaccine development

When the next influenza pandemic emerges, it will likely be caused by a type of influenza virus to which humans have little to no previous exposure. Vaccination offers one of the most effective measures for minimizing the morbidity and mortality of influenza. Inactivated influenza vaccines were developed more than 50 years ago, and since that time, annual vaccination with the inactivated vaccine has been the primary method by which the disease burden of influenza has been reduced. While influenza vaccines work well in the majority of people, they often do not work as well in the very young, the very old, or in patients with a compromised immune system. A live, attenuated vaccine against influenza was licensed in 2003 for use in individuals 5 to 49 years of age. During a pandemic with a novel influenza virus, public health officials will be confronted with making critical decisions about the vaccine dosage level and immunization regimen for various populations.

Vaccines produced in the event of the emergence and spread of a new pandemic influenza strain must be safe, able to be produced in large quantities and delivered quickly, and protect the largest number of individuals possible. Currently available influenza vaccines are produced by growing influenza viruses in embryonated chicken eggs, and take from 6 to 9 months to prepare. The rapid production and clinical evaluation of investigational lots of pandemic vaccines is an urgent global public health priority.

Goals:

- Increase availability of safe, effective, licensed pandemic influenza vaccines.
- Expand the repository of available vaccines, including those with varying potencies.

Ongoing HHS activities:

- Preparing of reference viruses of pandemic potential
- Preparing candidate vaccine reassortant strains for inactivated and live attenuated vaccines

Vaccines produced in the event of the emergence and spread of a new pandemic influenza strain must be safe, able to be produced in large quantities and delivered quickly, and protect the largest number of individuals possible.

- Supporting preclinical and clinical studies of pandemic (e.g., H5N1, H9N2) inactivated and live attenuated vaccines
- Establishing small clinical trial networks in Southeast Asia in collaboration with WHO and others
- Developing alternatives to egg-based vaccine manufacturing technologies, which include cell culture-based systems, recombinant proteins, DNA-based platforms
- Developing common antigen vaccines, which could offer protection from multiple influenza viruses, including M2 Peptide-based vaccines
- Developing alternative mechanisms of vaccine administration, including nasal gel, topical patches, and self-administered vaccines
- Developing antigen-sparing strategies
- Supporting "Immune Modeling Centers" that use computational models to predict human immune responses to influenza and to test novel vaccine strategies
- Investigating genetic characteristics of influenza A and B viruses that influence virus yield in eggs and tissue culture

Future priorities:

- Evaluate strategies to enhance the yield of production of influenza vaccine using current manufacturing processes.
- Support the production and evaluation of investigational lots of pandemic vaccines, including those likely to be of greatest risk, to assess safety and immunogenicity in various populations.
- Continue development of new influenza vaccines, including those that may provide longer-term and/or broader protection.
- Assess the potency of existing vaccines against combinations of traditional vaccine targets, e.g., HA and NA from different strains.
- Explore the potential of more highly conserved viral genes as targets of vaccination, and the efficacy of combination strain vaccine.
- Develop gene-based vaccines against influenza.
- Assess the potential contribution of cellular immunity and broader cross-protection that may be provided by vaccination.
- Monitor the long-term sequelae of vaccination, including the possible protective role of vaccination against non-infectious diseases such as cardiovascular, neurological, and other diseases.
- Develop mass vaccination/delivery techniques.
- Develop common protein vaccines.
- Develop investigational live attenuated influenza virus vaccine candidates for all 16 antigenic subtypes of HAs (H1 to H16).

Performing clinical research during a pandemic offers a unique opportunity for gaining critical information about novel influenza infections.

H. Research resources and training

Supporting the availability of research resources is essential to facilitate advances in basic and translational research on influenza. These resources include providing research reagents and access to genomic and immunologic databases, animal models for preclinical drug and vaccine development, and biocontainment laboratories.

Goals:

- Regularly update and expand reagents and influenza virus sequence data available to the worldwide research community.
- Expand the number of well-trained investigators who have influenza research or surveillance as a primary focus.

Ongoing HHS activities:

- Preparing antibodies and reference antigens to avian influenza viruses considered to be of high pandemic potential
- Development of diagnostic tests such as real-time PCR for rapid diagnosis of potential pandemic viruses
- Training of Public Health Laboratories in detection and characterization of potential pandemic viruses (courses and bench training of national and international laboratorians)
- Conducting animal influenza surveillance training courses in Asia
- Supporting the Influenza Genome Sequencing Project to determine the complete genetic sequences of thousands of influenza virus isolates and to rapidly provide these sequence data to the scientific community

Future priorities:

- Produce purified reference antigens to each of the 16 novel influenza virus hemagglutinins and to selected neuraminidase molecules.
- Prepare subtype-specific reference antisera (monoclonal and/or polyclonal antibodies) to avian hemagglutinin and neuraminidase proteins for use in the rapid identification of novel viruses and vaccine standardization.
- Produce a series of oligonucleotide primers to conserved regions of influenza virus genomes. These primers would allow for the rapid sequencing, identification, and characterization of novel influenza virus strains.
- Establish mechanisms that facilitate collaboration among international laboratories, which could result in the sharing of reagents, virus strains, data, new technologic advances, and training of laboratory personnel.

I. Research priorities during a pandemic

In the face of novel infections including novel influenza viruses, the optimal treatment and public health management is not clear. In the absence of clinical trials evaluating a pandemic strain, anecdotal experience is often extrapolated to mandates on standards of care, even if the intervention has no proven utility and may be harmful. Performing clinical research during a pandemic offers a unique opportunity for gaining critical information about novel influenza infections. The information gained may help minimize the impact of future epidemics.

Goals:

- Provide public health policy-makers with data to guide a pandemic response.
- Provide clinicians with scientific data to justify recommended treatments, vaccines, or other interventions.

Future priorities:

- Evaluate change in natural history of disease and effect of antiviral drugs (including possible dosing changes, resistance emergence, adverse events and risk/benefit assessment, etc.) in management of pandemic strain compared to previously circulating strains.
- Evaluate the safety and immunogenicity of different doses of pandemic influenza vaccines in various populations.
- Assess risk factors for infection and person-to-person transmission.
- Evaluate the population impact of outbreaks early in the development of a pandemic.
- Evaluate the effect of interventions such as travel restrictions or school closings during outbreaks early in the development of a pandemic.
- Evaluate the effect of early use of antiviral drugs in high-risk patients.
- Evaluate the efficacy of the pandemic vaccine.
- Evaluate the impact of vaccination on pathogenesis and transmission.
- Evaluate the characteristics of diagnostic tests.
- Continue other ongoing research priorities (discussed in previous sections) to the extent compatible with the pandemic situation.
- Evaluate infection control measures to prevent or minimize the spread of pandemic influenza within healthcare settings.

J. Research priorities after a pandemic

Since influenza is a global infection affecting multiple species, it is unlikely that influenza can ever be eradicated. It is likely that future pandemics that occur will continue to affect people. Therefore, critical examination of plans, responses, and outcomes of the pandemic may afford information that could affect planning and minimize impact of future pandemics.

Goal:

- Evaluate the effectiveness of policies and procedures used in the pandemic.

Future priorities:

- Detail the "natural history" of the pandemic.
- Compare the effectiveness of different infection control policies.
- Determine the factors that influenced vaccination strategies.
- Compare different vaccine delivery systems for mass vaccination.
- Determine the different rates and risk factors for adverse events to pandemic strain of influenza vaccine.
- Evaluate antiviral and vaccination strategies.
- Assess adverse events related to antivirals and vaccines.
- Evaluate the most effective disease surveillance strategies.

appendix H: international partnership on avian and pandemic influenza

The newly formed International Partnership on Avian and Pandemic Influenza (IPAPI), announced by President Bush at the United Nations General Assembly on September 14, 2005, brings together countries that share a set of core principles to generate and coordinate political momentum for addressing avian and pandemic influenza. With commitment from the highest political levels in countries around the world, IPAPI will strive to improve international surveillance, transparency, timeliness, and response capabilities and facilitate sharing of epidemiological information and samples critical for the response effort.

The Senior Officials Meeting of IPAPI, held in Washington, DC, on October 7, 2005, launched the Partnership and led to a jointly developed plan of action for coordinating national activities, evaluating national capabilities and filling gaps. This plan, based on the partnership's core principles (below), will supplement ongoing and planned international efforts and support the work of the relevant international organizations, including the World Health Organization (WHO), the World Animal Health Organization (OIE), the United Nations Food and Agriculture Organization (FAO), and other international and regional bodies and the private sector, NGOs, and others.

At the first meeting of IPAPI **over 80 countries and 8 international organizations came together, endorsing the core principles and agreeing to follow up on a number of major policy issues** that need further discussion at the highest political levels to resolve concerns or gain true consensus so that necessary movement can occur. A summary document that identifies the issues of greatest policy significance for dealing with the threats of avian and pandemic influenza was developed. Sub-groups of partners will deal with these, so that by the middle of 2006, progress made in raising the political attention on the problem and addressing the issues identified will be reported. Countries will convene the meetings of the sub-groups to focus on the issues identified. These sub-groups will coordinate with the relevant international organizations on technical matters. The sub-groups will identify any gaps needing further attention, and additional sub-groups may form to address issues as they arise.

The **Core Principles** that underpin the Partnership are:

1. International cooperation to protect the lives and health of our people;
2. Timely and sustained high-level global political leadership to combat avian and pandemic influenza;
3. Transparency in reporting of influenza cases in humans and in animals caused by strains that have pandemic potential, to increase understanding, preparedness, and especially to ensure rapid and timely response to potential outbreaks;
4. Immediate sharing of epidemiological data and samples with the World Health Organization (WHO) and the international community to detect and characterize the nature and evolution of any outbreaks as quickly as possible by utilizing, where appropriate, existing networks and mechanisms;

Since pandemics are diseases without borders, the influenza virus will not respect political or geographic boundaries—a threat against one nation is a threat against the entire world.

5. Rapid reaction to address the first signs of accelerated transmission of H5N1 and other highly pathogenic influenza strains so that appropriate international and national resources can be brought to bear;
6. Prevent and contain an incipient epidemic through capacity building and in-country collaboration with international partners;
7. Work in a manner complementary to and supportive of expanded cooperation with and appropriate support of key multilateral organizations (WHO, Food and Agriculture Organization, World Organization for Animal Health);
8. Timely coordination of bilateral and multilateral resource allocations, dedication of domestic resources (human and financial), improvements in public awareness, and development of economic and trade contingency plans;
9. Increased coordination and harmonization of preparedness, prevention, response, and containment activities among nations, complementing domestic and regional preparedness initiatives and encouraging where appropriate the development of strategic regional initiatives;
10. Actions based on the best available science.

This Partnership will help us improve international surveillance, transparency, timeliness, and response capabilities. Since pandemics are diseases without borders, the influenza virus will not respect political or geographic boundaries—a threat against one nation is a threat against the entire world. This initiative will strive for complete transparency, rapid response capabilities, cooperative surveillance, and will facilitate the sharing of epidemiological data and samples with each other and with the relevant international organizations. This will give us commitment from the highest political levels in countries around the world to adhere to these principles.

Future activities

In addition to participating in IPAPI, HHS will continue to work with other governments, international organizations such as GHSAG and WHO, the newly appointed UN Secretary-General's Special Representative on Pandemic Influenza, and other U.S. agencies individually as part of the overall USG international strategy. We will pursue a diplomatic strategy and provide technical assistance to affected countries and countries at risk. We will provide additional funding in FY 06 and thereafter, building on the work we are doing now in Southeast Asia. We expect to broaden our coverage to other parts of the globe. We will continue to look for increasing human-to-human transmission anywhere in the world as a triggering event for initiating a pandemic response by the U.S. HHS will pursue a prevention approach if possible, and a containment strategy where feasible—acting in concert with WHO and other nations as appropriate. At the core of this strategy, basic public health measures will be essential in reducing transmission in affected countries.

appendix I: acronym list

Abbreviations and Acronyms

ACF.....Administration for Children and Families

ACIP.....Advisory Committee on Immunization Practices

ASH.....Assistant Secretary for Health

ASPA.....Assistant Secretary for Public Affairs

ASPHEP.....Assistant Secretary for Public Health Emergency Preparedness

ASTHO.....Association of State and Territorial Health Officials

CDC.....Centers for Disease Control and Prevention

CONOPS.....Concept of Operations

DHS.....Department of Homeland Security

DoD.....Department of Defense

EOC.....Emergency Operations Center

ESF.....Emergency Support Function

FDA.....Food and Drug Administration

FEMA.....Federal Emergency Management Agency

FMCS.....Federal Medical Contingency Stations

HA.....hemagglutinin (a protein on the surface of the influenza virus)

HHS.....Department of Health and Human Services

HRSA.....Health Resources and Services Administration

HSPD.....Homeland Security Presidential Directive

ICS.....Incident Command System

IIMG.....Interagency Incident Management Group

ILI.....influenza-like-illness

IOM.....Institute of Medicine

NA.....neuraminidase (a protein on the surface of the influenza virus)

NI.....neuraminidase inhibitors

NIC.....National Influenza Center

NIH .....National Institutes of Health

NDMS.....National Disaster Medical System

NIMS .....National Incident Management System

NRP.....National Response Plan

NVAC.....National Vaccine Advisory Committee

NVPO/HHS .....National Vaccine Program Office, Department of Health and Human Services

OPHEP/HHS .....Office of Public Health Emergency Preparedness, Department of Health and Human Services

OGHA/HHS .....Office of Global Health Affairs, Department of Health and Human Services

OIGA/HHS .....Office of Intergovernmental Affairs, Department of Health and Human Services

PHS .....Public Health Service

PPE.....Personal Protective Equipment

R&D .....Research and Development

SARS.....Severe Acute Respiratory Syndrome

USAID.....U.S. Agency for International Development

USDA.....U.S. Department of Agriculture

VRBPAC .....Vaccine and Related Biological Products Advisory Committee

WHO.....World Health Organization

appendix J: internet resources on pandemic influenza

The links listed below were active as of October 2005. However, because Web sites can change without notice, no site can be guaranteed active or accurate indefinitely.

U.S. Government

www.pandemicflu.gov

Nongovernmental Organizations

Association of State and Territorial Health Officials (ASTHO) – www.astho.org

Infectious Disease Society of America – www.idsociety.org

National Foundation for Infectious Diseases – www.nfid.org

Institute of Medicine (IOM) – www.iom.edu

World Health Organization (WHO) – www.who.org

Influenza background information

CDC – Presents information on the symptoms, treatment, and complications of the disease, prevention and control, the types of influenza viruses, questions and answers on symptoms, vaccination. and myths. www.cdc.gov/flu

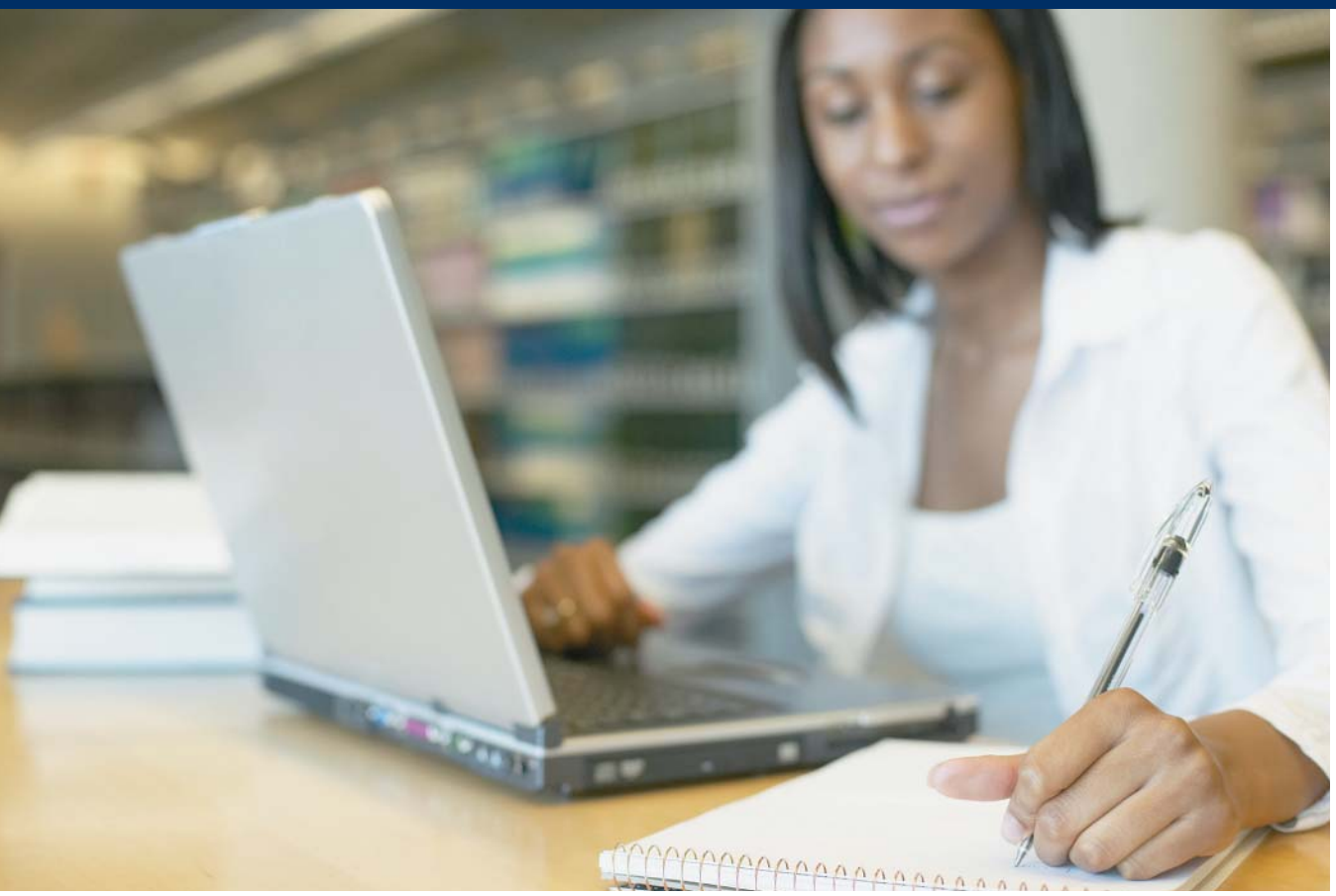
National Vaccine Program Office – Presents a historical overview of pandemics that occurred throughout the past century (Spanish Flu, Asian Flu, Hong Kong Flu), and three influenza scares (Swine Flu, Russian Flu, and Avian Flu). www.dhhs.gov/nvpo/pandemics

World Health Organization – Defines an influenza pandemic, explains how a new influenza virus can cause a pandemic, presents the consequences of an influenza pandemic, explains the global surveillance systems, and provides links to other pandemic plans from other nations. www.who.int/csr/disease/influenza/pandemic/en

Additional response resources

HRSA Bioterrorism and Emergency Preparedness Grants and Cooperative Agreements – Provides information about HRSA programs for bioterrorism and emergency preparedness activities available for state and local jurisdictions. www.hrsa.gov/bioterrorism

www.pandemicflu.gov



The Public Health Preparedness and Response Capacity Inventory – Provides a resource for state and local health departments undertaking comprehensive assessments of their preparedness to respond to bioterrorism, outbreaks of infectious disease, or other public health threats and emergencies. www.dhs.ca.gov/epo/PDF/NPSsmpxv1.pdf

CDC Cooperative Agreements on Public Health Preparedness – Provide funding to state and local public health jurisdictions for preparedness for and response to bioterrorism, other outbreaks of infectious diseases, and other public health threats and emergencies. www.bt.cdc.gov/planning/continuationguidance

Epidemic Information Exchange – Provides a secure, web-based communications network for information exchange among CDC, state and local health departments, and other public health professionals. www.cdc.gov/mmwr/epix/epix.html

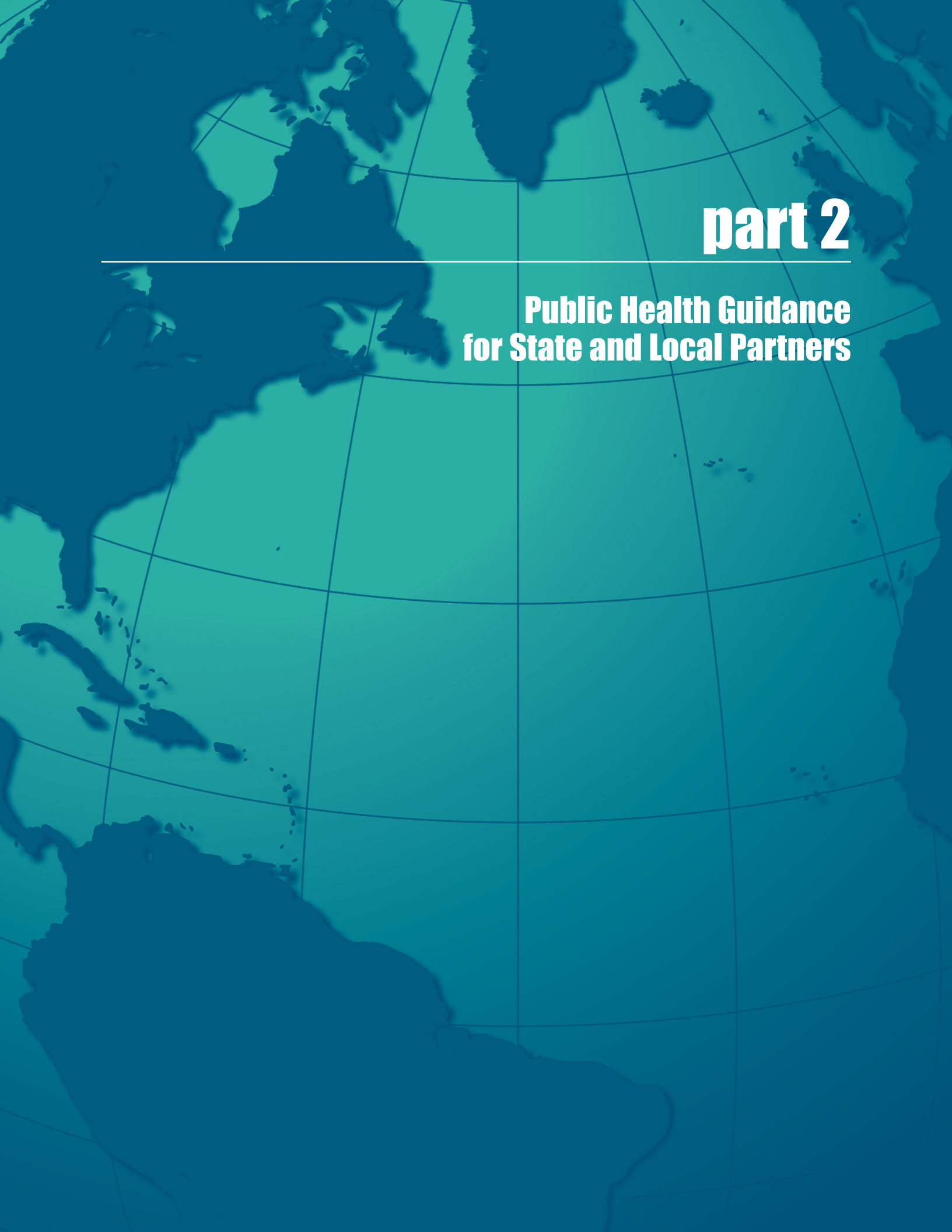
Centers for Public Health Preparedness – A national system for competency-based training tools for the public health workforce. www.asph.org/acphp

Strategic National Stockpile – Provides information on the availability and rapid deployment of life-saving pharmaceuticals, antidotes, other medical supplies, and equipment necessary to counter the effects of nerve agents, biological pathogens, and chemical agents. www.bt.cdc.gov/stockpile

Smallpox Response Plan and Guidelines (Version 3.0) – Presents the most current criteria for implementation of CDC smallpox response plan, notification procedures for suspected smallpox cases, CDC and state/local responsibilities and action in the event of a smallpox outbreak, vaccine mobilization and deployment, and CDC personnel mobilization and deployment. www.bt.cdc.gov/agent/smallpox/response-plan

FDA, Center for Biologics Evaluation and Research - Discussion of influenza vaccines and related information. www.fda.gov/cber/flu/flu.htm

FDA, Center for Drug Evaluation and Research – Discussion of influenza antiviral drugs and related information. www.fda.gov/cder/drug/antivirals/influenza



part 2

Public Health Guidance for State and Local Partners

introduction

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PART 2. PUBLIC HEALTH GUIDANCE ON PANDEMIC INFLUENZA FOR STATE AND LOCAL PARTNERS[1]

A. Introduction

An influenza pandemic may emerge with little warning, affecting a large number of people within a short space of time. During the first wave of the pandemic, outbreaks may occur simultaneously in many locations throughout the nation, preventing a targeted concentration of national emergency resources in one or two places—and requiring each locality to depend in large measure on its own resources to respond. A vaccine will not yet be available, and the supply of antiviral drugs will be limited. Local outbreaks may last for weeks or months, and widespread illness in a particular community could lead to shortages in the healthcare sector as well as in essential services.

An effective local response will depend on pre-established partnerships and collaborative planning by public health officials, hospital administrators, and community leaders, who have considered a range of best-case and worst-case scenarios. It will require flexibility and real-time decision-making, guided by epidemiologic information on the pandemic virus. It will also depend on a well-informed public that understands the dangers of pandemic influenza and accepts the potential need for control measures like self-isolation and quarantine that prevent disease spread by reducing social contact. The public must also understand and accept the rationale in prioritizing the use of limited supplies of antiviral drugs and initial stocks of vaccines.

The goal of Part 2 of the *HHS Pandemic Influenza Plan* is to help state and local jurisdictions and healthcare facilities mount an effective response to pandemic influenza. Public Health Guidance on Pandemic Influenza for State and Local Partners was developed with input from many public health and medical partners with front-line responsibility for pandemic influenza response.

Purpose and Aims

All U.S. state, local, and tribal governments must be prepared to detect the earliest cases of disease, to minimize illness and morbidity, and to decrease social disruption and economic loss. The principle aims of the *Public Health Guidance for State and Local Partners* are to:

- Provide guidance for updating state-level pandemic influenza response plans developed in fulfillment of activities under the CDC and HRSA Cooperative Agreements for Public Health Emergency Preparedness and Bioterrorism Hospital Preparedness (*www.bt.cdc.gov/planning/guidance05/index.asp* and *www.hrsa.gov/grants/preview/guidancespecial/hrsa05001.htm*).
- Help healthcare partners address the medical challenges of pandemic influenza (e.g., evaluation and management of large numbers of patients, occupational health risks, and limited supplies of antiviral medications and vaccines).
- Define the public health role in healthcare planning and preparedness for pandemic influenza.
- Strengthen linkages between public health departments and private sector partners—including healthcare facilities, community-based organizations, clinical laboratories, behavioral health experts, and first responders—to protect health and preserve essential services during a pandemic.

Many activities described in the Public Health Guidance for State and Local Partners are similar, if not the same as those required to combat other infectious diseases, such as Severe Acute Respiratory Syndrome (SARS) or intentionally-spread smallpox or plague. Topics covered in the *Public Health Guidance for State and Local Partners* may, therefore, be relevant to—or addressed in—other emergency preparedness plans. (See, for example: *Public Health Guidance for Community-Level Preparedness and Response to SARS:* www.cdc.gov/ncidod/sars/guidance/; *Smallpox Response Plan and Guidelines*: www.bt.cdc.gov/agent/smallpox/response-plan/index.asp).

[1] Through this document, the term "state and local" is inclusive of territorial and tribal governments and health authorities, as applicable.

Organization

Part 2 of the *HHS Pandemic Influenza Plan* provides an overview of

- Pandemic influenza preparedness and response planning by state and local governments (Section B)
- Community planning to support healthcare facilities on a city-wide or regional basis during an influenza pandemic (Section C)

Part 2 also includes eleven supplements that provide guidance on specific aspects of pandemic influenza planning and response:

Supplement 1: Pandemic Influenza Disease Surveillance

Supplement 2: Laboratory Diagnostics

Supplement 3: Healthcare Planning

Supplement 4: Infection Control

Supplement 5: Clinical Guidelines

Supplement 6: Vaccine Distribution and Use

Supplement 7: Antiviral Drug Distribution and Use

Supplement 8: Community Disease Control and Prevention

Supplement 9: Management of Travel-Related Risk of Disease Transmission

Supplement 10: Public Health Communications

Supplement 11: Psychosocial Workforce Support Services

The content of each supplement is summarized in Section D.

Priority activities in each Supplement are organized under the time periods laid out in the WHO classification system proposed in February 2005: the *Interpandemic Period,* the *Pandemic Alert Period,* and the *Pandemic Period.* Some of the Supplements further subdivide Pandemic Period activities according WHO pandemic phases or to local levels of disease spread that will trigger particular activities over the course of the pandemic.

To help state and local public health and healthcare partners prepare for the unexpected, the *Public Health Guidance for State and Local Partners* includes a list of cross-cutting technical resources, including exercises and drills, to facilitate the exploration of different scenarios and local concerns (see **Supplement 3. Healthcare Planning,** Appendix 1). The *Public Health Guidance for State and Local Partners* also identifies disease-control issues whose resolution will require real-time guidance during a pandemic (Box 1).

Definitions of public health terms used throughout the *Public Health Guidance for State and Local Partners* are provided in Box 3 and in the Glossary.

B. Overview of Planning by State and Local Governments

All states and localities must be prepared to coordinate the pandemic influenza response within and between their jurisdictions. State and local responsibilities include:

- Enhancing disease surveillance to ensure early detection of the first cases of pandemic influenza in their jurisdictions (see **Supplements 1 and 2**).

- Distributing public stocks of antiviral drugs and vaccines and providing local physicians and hospital administrators with updated guidance on clinical management and infection control as the situation unfolds (**Supplements 3 to 7**[2])
- Preventing local disease transmission using a range of containment strategies (**Supplements 8 and 9**)
- Providing ongoing communication with the public (about the response effort, including the purpose and duration of containment measures) (**Supplement 10**)
- Providing psychological and social support services to emergency field workers and other responders (**Supplement 11**)

As described in Part 1, the HHS will support affected states or jurisdictions during an influenza pandemic by:

- Conducting outbreak investigations, as requested
- Conducting epidemiologic and laboratory-based studies ("special studies")
- Providing ongoing information from the national influenza surveillance system on the pandemic's impact on health and the healthcare system
- Expanding supply of antiviral drugs by stimulating increased U.S. based production capacity
- Expanding U.S.-based production capacity for pandemic vaccine and working with manufacturers to ensure that pandemic vaccine is produced at full capacity
- Distributing public stocks of antiviral drugs and other medical supplies from the Strategic National Stockpile to the states
- Distributing public stocks of vaccines, when they become available
- Providing guidance on community containment strategies, including travel restrictions, school closings, and quarantine
- Communicating with the public via the news media
- Monitoring the response

Planning Process

The first step in the planning process for state and local governments is to establish a Pandemic Influenza Coordinating Committee to oversee preparedness planning and ensure integration with other emergency planning efforts. The membership of the Coordinating Committee should represent a range of disciplines and expertise in the public and private sectors (Box 2).

The Coordinating Committee should draft and formally adopt a pandemic influenza response plan that:

- Delineates the roles and responsibilities of state and local agencies and offices
- Builds on existing preparedness and response plans for bioterrorism events, SARS, and other infectious disease emergencies
- Addresses legal issues including those that affect hospital staffing, patient care, and quarantine (see below)
- Is periodically reviewed and updated

As part of the planning effort, the Coordinating Committee should:

- Help establish and promote community-based task forces that support healthcare institutions on a city-wide or regional basis (see Section C).
- Identify the authority responsible for state-level declaration of a public health emergency and for officially activating the pandemic influenza response plan.

[2] Supplements 3, 4, and 5 are primarily directed to healthcare providers and hospital administrators, while Supplements 6 and 7 are also directed to state and local health officials.

- Identify an overall coordinator to work with hospitals and communicating with medical and mental health personnel during a pandemic.
- Identify the jurisdiction's controlling authority over intrastate and interstate modes of transportation, which might be curtailed during a pandemic.
- Identify state and local law enforcement personnel who will assist in maintaining public order and enforcing control measures during a pandemic.
- Develop and reinforce relationships with local health authorities in adjoining jurisdictions.
- Make planning decisions on acquisition and distribution of antiviral drugs and vaccines, in accordance with HHS recommendations.
- Ensure that plans take into account tribal populations, where applicable.
- Conduct state-level "table top" exercises to test response capabilities.
- Encourage local jurisdictions to conduct exercises and drills.

Legal Preparedness

The Coordinating Committee should review state and local statutory provisions regarding:

- Laws and procedures for closing businesses or schools and suspending public meetings during a declared state of emergency
- Medical volunteer licensure, liability, and compensation laws for in-state, out-of-state, and returning retired and non-medical volunteers
- Quarantine laws and how they apply in a public health emergency
- Workers' compensation laws as they apply to healthcare workers and workers who provide essential services
- Reimbursement for workers placed in isolation or quarantine (if not addressed in sick leave policies)

Relevant federal law should be reviewed as well and statutes should he harmonized, as feasible.

Additional information on legal preparedness is provided in Appendices 1 and 2.

C. Overview of Community-wide Planning to Support Healthcare Facilities

Without special preparation, a large-scale pandemic could quickly overwhelm local healthcare facilities and resources. Although institutional planning by hospitals is essential (see Supplement 3), it is not sufficient. Hospitals depend on many organizations and groups—e.g., suppliers of food, drugs, and medical supplies, sanitation workers, and telephone companies—to accomplish their day-to-day tasks. If workforce illnesses and absences prevent these organizations from functioning normally during a pandemic, hospitals will be severely affected.

State health authorities should consider promoting the establishment of local pandemic influenza task forces that will ensure community readiness to provide emergency support to healthcare facilities on a city-wide or regional basis. Depending on the state, the task forces may be coordinated by municipal, county, or tribal health departments, or by regional public health offices. Task force activities should be integrated with state-wide planning efforts and should reflect common goals and principles for preparedness and response.

Each local task force should include representatives from hospitals, community service organizations, professional organizations of physicians, nurses, and pharmacists, home health care organizations, long term care facilities, federally qualified health centers (FQHC) and other healthcare safety net providers, emergency medical services (EMS), behavioral health

experts, and public health officials. The task forces should also include private sector partners who provide essential services such as food, electricity, and water. They may also include civil protection authorities such as the police, sheriff's departments, and firefighters.

During a pandemic, the task force would be responsible for coordinating health care activities within the community and should work with local health departments and hospitals to:

- Improve communication with medical care providers and health care organizations.
- Monitor local hospital resources (e.g., adult and pediatric hospital beds, intensive care unit beds, emergency department beds, medical supplies, respirators and other equipment, mortuary capacity).
- Address emergency healthcare staffing needs and other medical surge capacity issues.
- Encourage coordination among state and federal healthcare facilities, such as Veterans Administration hospitals, Indian Health Service facilities, and Department of Defense hospitals.
- Conduct contingency planning with:
  - Private sector groups that support hospital functions, to ensure continuity of operations during the pandemic. These groups may include medical supply companies, medical gas companies, companies that supply food and clean linens, and internet service providers.
  - Public utilities (water, electricity, gas, telephone, sanitation) to ensure continued service during the pandemic.
  - Local law enforcement agencies who can help maintain order if a hospital is overwhelmed by a large volume of patients (ill or worried about being ill).
  - Identify alternative care sites for patient care (child and adult) and sites for quarantine.
  - Identify community-based organizations that can provide psychological and social support to healthcare workers, public health field workers, and other emergency responders (see **Supplement 11**).

Community Planning in Rural Areas

Special efforts should be made to address pandemic planning issues in rural communities and other areas where emergency rooms and other resources for urgent care and emergency treatment are lacking. Without community-wide planning, a surge of pandemic influenza patients could force the closure of local outpatient healthcare clinics. Planning partners may include healthcare providers at outpatient clinics, federally qualified health centers (FQHCs),[3] IHS and tribal health care facilities, and other healthcare safety net providers[4] that deliver care to low-income and other vulnerable populations.

D. Public Health Guidance Supplements

The eleven Public Health Guidance supplements can be found on the following pages. An overview of each supplement is provided below.

Supplement 1. Pandemic Influenza Surveillance provides recommendations to state and local partners on virologic surveillance for influenza viruses and on epidemiologic (disease) surveillance to monitor the health impact of influenza

[3] A federally qualified health center (FQHC) is a type of provider defined by the Medicare and Medicaid statutes. FQHCs include health centers receiving grants under section 330 of the Public Health Service Act, certain tribal organizations, and clinics designated by HHS as FQHC Look-Alikes. More information may be found at: http://www.cms.hhs.gov/providers/fqhc/

[4] Health care safety net providers deliver care to low-income and other vulnerable populations, including the uninsured and those covered by Medicaid. Many of these providers have either a legal mandate or an explicit policy to provide services regardless of a patient's ability to pay (http://www.ahcpr.gov/data/safetynet/faq.htm). Major safety net providers include public hospitals and community health centers as well as teaching and community hospitals, and private physicians.

(outpatient, hospital, and mortality surveillance). The Interpandemic and Pandemic Alert Period recommendations focus on disease surveillance during regular influenza seasons, as well as on surveillance for human cases of infection with avian influenza A (H5N1) or other novel strains of influenza. They also address preparedness planning to lay the groundwork for enhanced disease surveillance during a pandemic.

The Pandemic Period Recommendations focus on surveillance activities that will be undertaken if a pandemic virus is reported overseas or if a pandemic virus emerges in or enters the United States. These activities include ongoing virologic surveillance to monitor genetic and antigenic changes in the pandemic virus, including changes in its drug susceptibilities.

Supplement 2. Laboratory Diagnostics provides recommendations to state and local public health partners on the use of diagnostic tests to detect, characterize, and monitor novel subtypes of influenza, including avian influenza A (H5N1) and other viruses with pandemic potential. The Interpandemic and Pandemic Alert Period recommendations focus on laboratory testing in support of seasonal influenza surveillance, on laboratory-based detection of novel subtypes of influenza, and on preparedness planning to support the laboratory component of the response to an influenza pandemic (e.g., detection and characterization of viruses, case reporting, specimen management, and surge capacity issues).

The Pandemic Period recommendations focus on provision of laboratory support for disease surveillance and for clinicians and hospitals. The Pandemic Period Recommendations also cover occupational health issues for laboratory workers.

Supplement 3. Healthcare Planning provides guidance to healthcare partners on developing effective institutional plans for responding to an influenza pandemic. It focuses on Interpandemic Period guidance for healthcare preparedness planning in such areas as pandemic influenza surveillance, incident management infrastructure, hospital communications, education and training, patient triage, clinical evaluation and admission, facility access, occupational health, vaccine and antiviral drug use, surge capacity, and mortuary issues. Also considered is planning for providing care in non-hospital settings including clinics, physician's offices, and the alternative care sites that will be set up if hospital-bed capacity is exceeded during a pandemic.

The Pandemic Period guidance recommendations focus on activation of institutional pandemic influenza response plans.

Supplement 4. Infection Control provides recommendations to healthcare and public health partners on basic principles of infection control for limiting the spread of pandemic influenza. These principles are common to the prevention of other infectious agents spread by respiratory droplets. Guidance is included on the selection and use of personal protective equipment, hand hygiene, safe work practices, cleaning and disinfection of environmental surfaces, handling of laboratory specimens, and postmortem care. The guidance also covers infection control practices related to the management of infectious patients, the protection of persons at high-risk for severe influenza or complications, and issues concerning occupational health.

Supplement 4 also provides guidance on how to adapt infection control practices in specific healthcare settings, including hospitals, nursing homes and other long-term care facilities, pre-hospital care (Emergency Medical Services), home healthcare, and medical offices and other ambulatory care settings. The section on hospital care covers detection of entering patients who may be infected with pandemic influenza, implementation of source-control measures to limit virus dissemination from respiratory secretions, hospitalization of pandemic influenza patients, and detection and control of nosocomial transmission. Supplement 4 also includes recommendations on infection control measures and care of pandemic influenza patients in the home, as well as in alternative care sites that may be established if local hospital capacity is overwhelmed by a pandemic.

Given some uncertainty about the characteristics of a new pandemic strain, all aspects of preparedness planning for pandemic influenza must allow for flexibility and real-time decision-making that take new information into account as the situation unfolds. If the new virus is unusual in transmissibility, virulence, or in any other way, HHS and its partners will provide state and local partners with updated infection control guidance.

Supplement 5. Clinical Guidelines focus on the initial screening and clinical assessment of patients who present from the community with fever and/or respiratory symptoms during the Interpandemic, Pandemic Alert, and Pandemic Periods. The Appendices include information on the clinical presentation and complications of influenza, the clinical features of human infection with avian influenza A (H5N1), and management of secondary bacterial pneumonia during a pandemic.

During the Interpandemic and Pandemic Alert Periods, early recognition of an illness caused by a novel influenza strain will rely on a combination of clinical and epidemiologic features. During the Pandemic Period (with a setting of high community prevalence) diagnosis will likely be more clinically oriented, as exposure history will become less helpful and the likelihood will be high that any severe influenza-like illness would be pandemic influenza.

Supplement 6. Vaccine Distribution and Use provides recommendations to state and local partners and other stakeholders on planning for the different elements of a pandemic vaccination program. The focus of the Interpandemic Period recommendations is on planning for vaccine distribution, vaccination of priority groups, adverse event monitoring, tracking of vaccine supply and administration, vaccine coverage and effectiveness studies, communications, legal preparedness, and training. The focus of Pandemic Period recommendations is on working with public health and healthcare partners to implement plans for vaccine distribution and use.

Supplement 7. Antiviral Drug Distribution and Use provides recommendations to state and local partners on the distribution and use of antiviral drugs for treatment and prophylaxis during an influenza pandemic. The Interpandemic and Pandemic Alert Period recommendations focus on preparedness planning for rapid distribution and use of antiviral drugs (e.g., procurement, distribution to priority groups, legal preparedness, training, and data collection on use, effectiveness, safety, and the development of drug resistance). The Interpandemic and Pandemic Alert Period recommendations also cover the use of antiviral drugs in management and containment of cases and clusters of infection with novel strains of influenza, including avian influenza A (H5N1) and human strains with pandemic potential.

The Pandemic Period recommendations focus on local use of antiviral drugs in three situations: when pandemic influenza is reported abroad, when there is limited transmission of pandemic influenza in the United States, and when there is widespread transmission in the United States. Recommendations for optimal use of limited stocks of antivirals will be updated throughout the course of an influenza pandemic, in accordance with new epidemiologic and laboratory data. National recommendations will also be updated as an effective pandemic influenza vaccine becomes available.

Supplement 8. Community Disease Control and Prevention provides recommendations to state and local partners on the use of disease containment strategies to prevent disease transmission at different phases of an influenza pandemic. The Interpandemic and Pandemic Alert Period recommendations focus on preparedness planning for implementation of containment measures. They also outline actions that may be taken during the earliest stage of a pandemic when the first potential cases or disease clusters are detected. In this setting, relatively intense individual-level containment measures (e.g., patient isolation and identification, monitoring, and quarantine of contacts) may be used without causing undue strain on limited public health and health care resources.

The Pandemic Period recommendations focus on measures that may be beneficial and practical when there is a large number of cases and extensive viral transmission. In such a setting, individual-level measures may no longer be effective or feasible (e.g., if hospital isolation beds can no longer accommodate all patients, if most contacts cannot be traced in time to prevent further exposures, or if staffing constraints make contact-tracing impractical). In that case, state and local health departments may consider measures that decrease social contact within groups or whole communities (e.g., quarantine of groups of exposed persons, cancellation of public events, snow days, self-shielding, or widespread community quarantine). Effective use of community containment measures during a pandemic will require continuous evaluation of such parameters as viral transmissibility, the number and geographic distribution of cases, the reproductive rate of epidemic propagation, and the nature and severity of illness.

Supplement 9. Management of Travel-Related Risk of Disease Transmission provides recommendations to state and local partners on travel-related containment strategies that may be employed during different phases of an influenza pandemic. These strategies range from distribution of health alert notices, to isolation and quarantine of new arrivals, to restriction or cancellation of nonessential travel. State and local health departments will implement these strategies in association with Quarantine Stations located at 11 ports of entry.

The Interpandemic and Pandemic Alert Period recommendations focus on preparedness planning, as well as on management of arriving ill passengers on international flights or cruise ships. The Pandemic Period recommendations focus on travel-related measures to prevent disease spread into, out of, or within the United States.

Supplement 10. Public Health Communications describes seven key risk communications concepts. During the Interpandemic Period, national, state, and local health communications professionals should focus on preparedness planning and on building flexible, sustainable communications networks. During the Pandemic Alert Period, they should work collaboratively to develop and disseminate consistent and accurate messages. During the Pandemic Period, they should focus on well-coordinated health communications to support public health interventions designed to help limit influenza-associated morbidity and mortality and to address related social and economic changes.

Supplement 11. Psychosocial Workforce Support Services addresses the psychological and social ("psychosocial") needs of occupational groups who participate in the response to an influenza pandemic. These groups include:

- Healthcare workers who provide medical care for the children and adults who fall ill
- Emergency field workers and other public health personnel who help control disease spread
- First responder or non-governmental organizations whose employees assist affected groups (e.g., quarantined persons or patients at home or in hospitals)
- Essential service workers whose activities maintain normal social functions and minimize social disruption
- The family members of all of these groups

Recommendations for the Interpandemic and Pandemic Alert Periods focus on institutionalization of psychosocial support services that help workers manage emotional stress and resolve personal, professional, and family issues related to the response to an influenza pandemic. They also cover preparation of informational materials for distribution to employees and their families during the emergency. Finally, they cover the development of Workforce Resilience Programs that include assistance for families of responders who may be deployed in the field and inaccessible for extended periods of time.

Recommendations for the Pandemic Period focus on delivery of psychosocial support services to response workers, on provision of occupational health information to healthcare providers, and on implementation of Workforce Resilience Programs.

BOX 1. ISSUES FOR STATE AND LOCAL PARTNERS THAT WILL REQUIRE REAL-TIME GUIDANCE DURING A PANDEMIC

- What are the case definitions for suspected and confirmed cases of pandemic influenza? What types of epidemiologic data should be collected? (The answers may change over time, depending on the characteristics of the pandemic virus and the geographical spread of the pandemic.)
- What are the drug susceptibilities of the pandemic virus?
- What amounts of antiviral drugs are available to your state from public and private stocks?
- What amounts of pandemic influenza vaccine are available to your state from public stocks?
- Which groups of people are at greatest occupational and medical risk (i.e., what are the age-specific and occupational attack rates)? What modifications should be made to the national recommendations for distribution and use of antiviral drugs and vaccines to reflect this information?
- Which laboratory tests may be used locally for laboratory confirmation of pandemic-influenza cases? Which isolates should be sent to CDC for subtyping?
- How fast is the pandemic spreading in your area? What does local surveillance data on the number of hospitalizations and deaths suggest in regard to:
  - Distribution of hospital supplies and hospital beds on a regional or statewide basis
  - How fast local and regional hospital resources are being depleted
  - Implementation of school closings and other community containment measures
  - Situating and opening alternative care sites and quarantine facilities
  - Absentee rates at hospitals and at businesses that provide essential services
  - Impact of the outbreak on the public health and medical workforce
- Is anything unusual or unexpected? If so, should any modifications be made in infection control practices or in the detection or management?
- Is there evidence from statistical modeling that predicts where and how fast the pandemic will spread?

BOX 2. ESTABLISHING A PANDEMIC INFLUENZA COORDINATING COMMITTEE FOR STATE-LEVEL PLANNING

Coordinating Committee members may include:

- Representatives from the Governor's Office (supplemented by representatives of the mayor's office for large metropolitan areas)
- Representatives from local, county, or district health departments
- Representatives from territorial and tribal health departments
  - State Epidemiologist
  - State Laboratory Director
- Public Health Information Officer
- Public Affairs/Communications Officer
- Immunization Project Director
- State Strategic National Stockpile (SNS) Coordinator
- Representatives from:
  - State and Local Offices of Emergency Preparedness
  - State Mental Health Office
  - State Transportation Office
  - Office of the General Counsel at the state health department
- Representatives from HRSA and CDC

Membership of the Pandemic Influenza Coordinating Committee may overlap with state or local bioterrorism preparedness coordinating committees.

Stakeholders who provide input to the Coordinating Committee may include:

- Infectious disease physicians
- Public health and private clinical laboratories
- Immunization program personnel
- State public health associations or state associations of county and city health officials
- State primary care associations representing health centers in the state
- Hospitals and other healthcare facilities, including VA Hospitals, DoD Hospitals, and Indian Health Service facilities
- Medical societies and nursing organizations
- Pharmacists
- Community immunizers
- Emergency medical services and emergency departments within hospitals
- Local media officials

Additional participants may include

- Volunteer organizations involved in response and recovery to various disasters
- Social service agencies
- Law enforcement agencies
- Infectious disease experts from universities
- Funeral directors
- Local military installations
- Large industries or employers in the area
- State aviation authorities
- Representatives of public utilities
- Education administrators

BOX 3. INFLUENZA: INFORMATION AND DEFINITIONS

Influenza

- Influenza is an acute viral disease of the respiratory tract characterized by fever, headache, myalgia, prostration, coryza, sore throat, and cough. Otitis media, nausea, and vomiting are also commonly reported among children.
- For surveillance purposes, influenza-like illness (ILI) is defined as respiratory illness with temperature greater than 38°C plus either sore throat or cough.

Seasonal or Interpandemic Influenza

- Seasonal influenza occurs each winter, primarily causing self-limiting disease for 2 to 7 days in most infected individuals. Influenza complications—especially viral and bacterial pneumonias—can cause severe illness or death in infants, the elderly, the immunocompromised, and those with certain chronic medical conditions.
- As seasonal influenza viruses replicate and evolve, they develop small changes in their surface antigens that allow them to evade existing immunity to influenza in the human population. Influenza vaccines must therefore be reformulated each year to provide protection against currently circulating strains of influenza A and B.

Pandemic Influenza

- Pandemic influenza is an uncommon type of influenza A that causes greater morbidity and mortality than seasonal influenza. An influenza pandemic occurs when a new influenza A virus (a "pandemic influenza virus") emerges in the human population, causes serious illness, and then spreads easily from person to person worldwide. Influenza pandemics occurred three times during the twentieth century—in 1918, 1957, and 1968.

Novel Strains of Influenza

- Novel strains of influenza are newly identified influenza viruses that require close monitoring to determine whether they (or their genetic offshoots) are capable of pandemic spread. They may include avian or animal influenza strains that can infect humans (like avian influenza A [H5N1]), or new, or re-emergent, human viruses that cause cases or clusters of human disease.

APPENDIX 1. CHECKLIST OF LEGAL CONSIDERATIONS FOR PANDEMIC INFLUENZA

The following checklist is a planning tool highlighting the relevant partners, resources, planning considerations, due process considerations, and issues of legal liability and immunity that may arise in the context of pandemic influenza. Next to each consideration are listed the legal partners (e.g., public health, hospitals, public safety, emergency management, judiciary) who may be called upon to address these considerations as part of the affected community's response. The challenge of the public health response is to protect the health of many, while safeguarding the rights of the individual. An integrated and coordinated response by attorneys at all levels in the community is essential to achieving this goal.

The checklist format is not intended to set forth mandatory requirements or establish a national standard for legal preparedness. Each state and local jurisdiction should determine for itself whether it is adequately prepared for disease outbreaks in accordance with its own laws and procedures. Relevant federal law also should be reviewed and statutes harmonized, as feasible.

Planning Considerations

- ❑ Ensure that public health personnel have a basic understanding of the intersection among federal, state, local, and tribal laws regarding quarantine and isolation as they relate to international airports and interstate border crossings. [public health/public safety/emergency management]
- ❑ Where applicable, draft or update legal orders, motions, and templates requiring medical evaluation of non-compliant persons who meet the pandemic influenza case definition and have symptoms of pandemic influenza. [public health/hospitals]
- ❑ Ensure that legal counsel has reviewed the feasibility of requiring persons to self-monitor for medical conditions (e.g., temperature checks) and (where applicable) drafted legal orders or agreements. [public health]
- ❑ Ensure that legal counsel has reviewed the feasibility of issuing "exclusion" orders (i.e., excluding contacts from using public transportation, attending public meetings) and, where applicable, drafted templates and legal orders. [public health/public safety/emergency management]
- ❑ Ensure the existence of a statute, regulation, or other administrative mechanism authorizing isolation/quarantine for pandemic influenza. [public health/public safety/judiciary]
- ❑ Draft legal orders, motions, and templates for isolation/quarantine in homes, hospitals, or other designated facilities. [public health/hospitals/emergency management/public safety]
- ❑ Ensure that legal counsel has reviewed the feasibility of using electronic methods to monitor suspected non-compliant individuals in home isolation and/or quarantine. [public health/public safety]
- ❑ Ensure that legal counsel has reviewed draft legal orders, motions, and templates to quarantine facilities and to credential ingress and egress into such facilities. [public health/public safety/emergency management]
- ❑ Ensure that legal counsel has reviewed the feasibility of using faith-based organizations to assist or provide services to persons in isolation and quarantine. [public health]
- ❑ Ensure that public health officials have reviewed the availability of workers' compensation and/or other forms of financial support for persons unable to return to work because of an isolation/quarantine order. [public health]
- ❑ Ensure that legal counsel has considered whether the health department should issue documents designed to assist with reintegration of persons subject to isolation/quarantine order (e.g., letter to employer or school explaining that patient is no longer infectious). [public health]
- ❑ Ensure that legal counsel has reviewed agreements relating to overtime and/or flexibility of hours for staff. [public health/hospitals/public safety/emergency management]
- ❑ Ensure that legal counsel has a clear understanding of legal authorities relevant to environmental remediation of buildings. [public health/hospitals/emergency management]

Partnerships/Outreach

- ❑ Assemble a legal preparedness task force with representation from public health, public safety, hospitals, emergency management, judiciary, and other relevant individuals and/or organizations at various levels of authority (federal, state, tribal, local, cross-border). [public health/public safety/hospitals/emergency management/judiciary]
- ❑ Establish procedures for enforcement of isolation/quarantine orders. [public health/public safety]
- ❑ Provide public safety personnel with educational materials relating to pandemic influenza and have a clear understanding for how to enforce an isolation/quarantine order. [public health/public safety]
- ❑ Ensure that procedures or protocols exist between hospitals and public health to manage a possible or known pandemic influenza case-patient who attempts to leave the hospital against medical advice. [public health/hospitals/public safety]
- ❑ Where applicable, draft memoranda of agreement (MOA) or understanding (MOU) to allow for the loaning of facilities or other services necessary to implement a quarantine and/or isolation order for persons who cannot be isolated at home (e.g., travelers, homeless populations). [public health/hospitals/emergency management]
- ❑ Ensure that judges and attorneys in the area, through local bar organizations or other entities, have received educational materials, training, or information related to SARS and the potential use of isolation/quarantine to interrupt disease transmission. [public health/judiciary]
- ❑ Ensure that legal counsel has reviewed and/or drafted data sharing/data use/confidentiality agreements related to sharing of confidential patient medical information between public health and other partners. [public health/hospitals/public safety/emergency management]

Due Process Considerations

- ❑ Draft legal orders and templates using terms such as "quarantine," "isolation," and "detention" consistently. [public health/judiciary)
- ❑ Ensure that legal counsel has reviewed all draft isolation/quarantine orders and forms, as well as applicable administrative hearing procedures, to ensure concurrence with basic elements of due process (e.g., adequate notice, opportunity to contest, administrative determination). [public health/judiciary]
- ❑ Ensure that procedures or protocols exist to ensure that persons subject to an isolation/quarantine order have access to legal counsel, if desired (e.g., list of attorneys willing to provide services at little or no cost). [public health/judiciary]
- ❑ Ensure that legal counsel has analyzed procedures needed to satisfy due process in different isolation/quarantine scenarios (e.g., "voluntary" home isolation, isolation in a guarded facility, exclusion from certain public activities). [public health/judiciary]
- ❑ Where applicable, ensure that public health officials have worked with the local court system to develop a 24 hours a day, 7 days a week "on call" list of judges or hearing officers to review emergency requests for isolation/quarantine. [public health/judiciary]
- ❑ Ensure that public health officials have worked with the local court system to develop a plan for hearing cases and/or appeals for persons subject to isolation/quarantine orders (e.g., participation via telephone, video conference). [public health/judiciary]

Legal Resources and Statutes

- ❑ Ensure that legal counsel has reviewed and has a clear understanding of the legal resources and tools relevant to a community's public health response. [public health/judiciary/emergency management]

  Such resources and tools include:

  - Draft Model State Emergency Health Powers Act
    www.publichealthlaw.net/MSEHPA/MSEHPA2.pdf

- Emergency Management Assistance Compact (model agreement)
  http://www.emacweb.org/?13
- Emergency Management Assistance Compact (as implemented in a state or jurisdiction)
- Memorandum of Understanding for Establishment of Local Public Health Mutual Aid and Assistance System:
  www.publichealthlaw.net/Resources/ResourcesPDFs/MOU.pdf
- American Bar Association Draft Checklist for State and Local Government
  Attorneys to Prepare for Possible Disasters
  http://www.publichealthlaw.net/Resources/BTlaw.htm
- Legal Authorities for Isolation and Quarantine
  http://www.cdc.gov/ncidod/sars/legal.htm
- Quarantine and Isolation: Lessons Learned from SARS
  http://www.louisville.edu/medschool/ibhpl/images/pdf/SARS%20REPORT.pdf
- Checklists on Legal Preparedness for Bioterrorism and other Public Health Emergencies
  http://www.publichealthlaw.net/Resources/BTlaw.htm
- Legal Materials Related to Public Health Legal Preparedness
  http://www2a.cdc.gov/phlp/sub_menu.asp

Additional materials and resources may be posted at http://www.cdc.gov/phlp/index.htm

❑ Distribute draft letters or fact sheets to hospitals and other healthcare providers describing permissible uses and disclosures of health information for public health purposes under the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA) (www.hhs.gov/ocr/hipaa/). [public health/hospitals]

❑ Where applicable, ensure that legal counsel understands procedures for declaring a public health emergency (at various levels of government) and consequences of such a declaration. [public health/public safety/emergency management]

❑ Ensure that legal counsel is familiar with the requirements of the Emergency Medical Treatment and Active Labor Act (EMTALA) (www.aaem.org/emtala/index.shtml) and has determined if such requirements have been incorporated into public health and hospital planning for pandemic influenza. [public health/hospitals]

❑ Ensure that legal counsel has reviewed hospital screening and admission procedures for potential pandemic influenza patients (e.g., establishment of evaluation clinics for persons with influenza-like symptoms) for compliance with EMTALA. [public health/hospitals]

❑ Ensure that legal counsel has reviewed potential EMTALA implications of a community-wide EMS protocol for transport of pandemic influenza patients (e.g., protocol requiring transport of pandemic influenza patients to a hospital or facility other than the hospital that owns the ambulance). [public health/hospitals/emergency management]

Legal Liability and Immunity

❑ Ensure that legal counsel has reviewed the potential legal liability of implementing "working" quarantine for essential service personnel. [public health/hospitals]

❑ Ensure that legal counsel has reviewed the potential legal liability of housing pandemic influenza patients in home isolation with non-exposed residents subject to infection control precautions. [public health]

❑ Ensure that legal counsel has reviewed liability/immunity for volunteers providing assistance or services to persons in isolation/quarantine. [public health/emergency management]

❑ Ensure that legal counsel has reviewed hospital employment policies on emergency licensure and/or employment of retired or non-medical personnel or personnel from other medical departments or hospitals. [public health/hospitals]

APPENDIX 2. FACT SHEET: PRACTICAL STEPS FOR LEGAL PREPAREDNESS

Step 1: Know your legislation

State and local public health officers need to be familiar with the legal requirements in their jurisdictions regarding isolation of infectious persons and quarantine of exposed persons. Although most states have laws to compel isolation and/or quarantine, procedures may vary widely from jurisdiction to jurisdiction. Key persons, such as legal counsel, judges, and policymakers, should be identified and made part of your jurisdiction's planning for pandemic influenza.

HHS has statutory authority, which has been delegated to CDC, to quarantine or isolate individuals who have been exposed to or infected with pandemic influenza. President Bush added pandemic influenza to the list of quarantineable diseases by Executive Order 13375 on April 1, 2005.

Step 2: Plan "due process"

Procedural due process is implicated when the government seeks to deprive an individual of "liberty" interests within the meaning of the Due Process Clause of the Fifth or Fourteenth Amendment to the U.S. Constitution. Many states, through statute or regulation, have established specific administrative and judicial schemes for affording due process to a person subject to a quarantine and/or isolation order. Schemes in other jurisdictions may not directly address this issue.

Although due process is a flexible concept and calls for procedural protections as the particular situation demands, the basic elements of due process include: adequate notice (typically through written order) of the action the agency seeks to compel; right to be heard (typically through the right to present evidence and witnesses and to contest the government's evidence and witnesses); access to legal counsel; and a final administrative decision that is subject to review in a court of law. These due process protections should not impede the immediate isolation or quarantine of an individual for valid public health reasons in an emergency situation.

Step 3: Draft key documents in advance

State and local public health officers should consider drafting key documents in advance of an emergency. These template documents can be critical time savers in an emergency. Documents that jurisdictions should consider preparing in advance include: draft quarantine and/or isolation orders; supporting declarations and/or affidavits by public health and/or medical personnel; and an explanation of the jurisdiction's due process procedures for persons subject to an isolation/quarantine order. Examples of documents created by other jurisdictions are found at: http://www.cdc.gov/phlp/index.htm

Step 4: Contact other jurisdictions

It is possible for federal, state, tribal, and local health authorities simultaneously to have separate but concurrent legal quarantine power in a particular situation (e.g., an arriving aircraft at a large city airport). Furthermore, public health officials at the federal, state, tribal, and local level may occasionally seek the assistance of their respective counterparts, e.g., law enforcement, to assist in the enforcement of a public health order. State and local public health officers should therefore be familiar with the roles and responsibilities of other jurisdictions: vertically (local, state, tribal, federal), horizontally (public health, law enforcement, emergency management, and health care), and in geographical clusters (overlapping state/local neighbors).

Step 5: Engage the courts in advance

Some jurisdictions may rely on older public health statutes that have not been amended in over half a century, while other jurisdictions may have recently revised their legal authorities to respond to bioterrorism or other public health emergencies. Judges who may be called upon to review a public health order may not be familiar with the state or local health authority's

broad public health powers. During the 2003 SARS outbreak in Toronto, Canada, for example, many judges were unaware of the health officer's broad ex parte authority to compel isolation/quarantine under rarely used laws.

Step 6: Anticipate practical problems

State and local public health officers need to be prepared for the practical problems that may arise in affording adequate due process protections to persons subject to isolation and/or quarantine orders. Such problems may include how to arrange for the appearance and representation of persons in quarantine (e.g., video conference or other remote means); how to serve an isolation/quarantine order (likely through law enforcement) and other procedures to advise persons of their legal rights; and isolation arrangements for transient or homeless populations.

Step 7: Communication

Communication planning is vital not only for an effective public health response but also for an effective legal response to a public health emergency. Public health agency counsel should be aware of media training available to other public health officers. During the SARS and monkeypox outbreaks, CDC, through the Public Health Law Program (http://www.cdc.gov/phlp/index.htm), established telephone conferences for public health legal counsel to share experiences and engage in peer-to-peer consultations. Efforts are now underway to develop materials to assist state and local public health departments in conducting further outreach on emergency public health issues to the legal community through local bar associations.

supplement 1
pandemic influenza surveillance

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SUMMARY OF PUBLIC HEALTH ROLES AND RESPONSIBILITIES IN PANDEMIC INFLUENZA SURVEILLANCE

INTERPANDEMIC AND PANDEMIC ALERT PERIODS

State and local responsibilities:

- Continue to employ state influenza surveillance coordinators to oversee improvements in influenza surveillance (e.g., virologic, outpatient, hospitalization, and mortality surveillance).
- Conduct influenza surveillance year round, where possible.
- Implement enhanced surveillance for detection of the first U.S. cases of novel virus infection.

State and large local public health laboratory responsibilities:

- Isolate and subtype influenza viruses year round.
- Improve capacity for rapid identification of unusual influenza strains (see also **Supplement 2**).

HHS responsibilities:

- Coordinate and maintain all components of the National Influenza Surveillance System (Table 1).
- Help identify and characterize influenza strains collected by the U.S. WHO Collaborating Laboratory Network.
- Assist USDA, as requested, in monitoring new influenza strains in poultry and swine.
- Work with state and local partners to:
  - Implement enhancements to the National Influenza Surveillance System.
  - Explore options for additional enhancements to improve pandemic surveillance.

PANDEMIC PERIOD

If an influenza pandemic begins in the United States or another country:

State and local responsibilities:

- Implement enhanced surveillance for detection of the first cases.
- Enhance all influenza surveillance components (virologic, outpatient, hospitalization, and mortality).
- Communicate to all partners the heightened need for timely and complete surveillance data.

HHS responsibilities:

- Provide technical support, as requested, to ministries of health and WHO to track the pandemic virus and gather epidemiologic data on risk factors for infection or severe illness.
- Issue updated case definitions and guidance for laboratory testing and enhanced surveillance.
- Assist state and local health departments, as requested.
- Analyze influenza surveillance data on a regular and timely basis.

S1-I. RATIONALE

Pandemic influenza surveillance includes surveillance for influenza viruses (virologic surveillance) and surveillance for influenza-associated illness and deaths (disease surveillance).

The goals of virologic surveillance are to:

- Rapidly detect the introduction and early cases of a pandemic influenza virus in the United States.
- Track the virus' introduction into local areas.
- Monitor changes in the pandemic virus, including development of antiviral resistance.

The goals of disease surveillance are to:

- Serve as an early warning system to detect increases in influenza-like illness (ILI) in the community.
- Monitor the pandemic's impact on health (e.g., by tracking outpatient visits, hospitalizations, and deaths).
- Track trends in influenza disease activity and identify populations that are severely affected.

Virologic and disease surveillance data—supplemented by data from outbreak investigations and special studies—can help decision-makers identify effective control strategies and re-evaluate recommended priority groups for vaccination and antiviral therapy. They can also facilitate efforts to mathematically model disease spread during a pandemic. The national influenza surveillance system, which monitors seasonal influenza, will provide the virologic and disease surveillance data needed to guide response efforts during a pandemic (www.cdc.gov/flu/weekly/fluactivity.htm; Table 1). When a pandemic begins, some enhancements might be instituted to improve geographic and demographic coverage and increase the amount of detail captured by particular components of the national influenza surveillance system.

S1-II. OVERVIEW

Supplement 1 provides recommendations to state and local partners on surveillance for influenza viruses and on disease surveillance to monitor the health impact of influenza. The recommendations for the Interpandemic and Pandemic Alert Periods focus on disease surveillance during interpandemic influenza seasons, as well as on surveillance for human cases of infection with avian influenza A (H5N1) or other novel strains of influenza. They also address preparedness planning for enhanced disease surveillance during a pandemic. The recommendations for the Pandemic Period focus on surveillance activities that will be undertaken if a pandemic virus is reported outside the United States or if a pandemic virus emerges in or enters the United States.

Outbreak investigations and special studies (e.g., to address questions about viral transmission or the clinical course of disease) are described in Part 1. Efforts to monitor the effectiveness and safety of vaccines and antiviral drugs are addressed in **Supplement 6** and **Supplement 7**.

The U.S. Department of Agriculture (USDA), through its Animal and Plant Health Inspection Service (APHIS), Veterinary Services (VS) program, works with the states and the agricultural industry to conduct influenza surveillance in domestic animals. USDA also monitors wild avian populations for highly pathogenic avian influenza (HPAI) and other diseases of concern through the APHIS Wildlife Services program. Active and passive surveillance for influenza A viruses in poultry in the United States have increased substantially since the outbreak of HPAI in Pennsylvania and surrounding states in 1983 and 1984.

S1-III. RECOMMENDATIONS FOR THE INTERPANDEMIC AND PANDEMIC ALERT PERIODS

CDC maintains and coordinates a national influenza surveillance system that identifies circulating influenza viruses and monitors disease activity during interpandemic influenza seasons. The seven components of the national influenza surveillance system—whose participants include healthcare providers, vital statistics offices, and local and state health departments and

public health laboratories—are listed in Table 1 and described in detail in Appendix 1. Components address virologic surveillance to determine when, where, and which influenza viruses are circulating, details of the various types of disease surveillance, and an overall state-level assessment of influenza activity.

A. Virologic surveillance during interpandemic influenza seasons

Public health goals for routine surveillance of influenza viruses are to identify and characterize circulating strains to inform annual vaccine formulation and to identify and characterize strains with pandemic potential. State and local public health laboratories, Department of Defense (DOD) laboratories, and clinical laboratories (including hospital and private commercial laboratories) should continue to participate in surveillance for influenza viruses through the U.S.-based collaborating laboratories of the World Health Organization (WHO) Global Influenza Surveillance Network and the National Respiratory and Enteric Virus Surveillance System (NREVSS) (see **Supplement 2)**. The aim of the network of WHO and NREVSS laboratories is to monitor influenza trends and compare seasonal differences, rather than to record all influenza tests performed in the United States. Network enhancements that might be useful during the Pandemic Period are discussed below (see S1-III.E).

B. Disease surveillance during interpandemic influenza seasons

1. National influenza surveillance system

The public health goals of influenza disease surveillance are to serve as an early warning system and to detect increases in ILI at the local level, to monitor the impact of influenza on health (e.g., by tracking outpatient visits, hospitalizations, and deaths), and to track trends in influenza disease activity and identify populations that are severely affected. During the Interpandemic Period, these goals are accomplished through the components of the national influenza surveillance system (Table 1). Public health and healthcare partners should continue to participate in these components of the national influenza surveillance system, which address the following types of disease surveillance.

a) Outpatient surveillance

- Sentinel Provider Network (SPN). Approximately 2,300 healthcare providers nationwide report the number of weekly outpatient visits for ILI and submit specimens from a small subset of patients to state public health laboratories for influenza virus testing.

b) Hospital surveillance

- Emerging Infections Program (EIP) influenza project. Laboratory-confirmed influenza-associated hospitalizations of children aged <18 years are monitored in 11 communities and reported to CDC on a bi-weekly basis.
- New Vaccine Surveillance Network (NVSN). Laboratory-confirmed influenza-associated hospitalizations of children aged <5 years are monitored in three communities and reported to CDC on a bi-weekly basis.

c) Mortality surveillance

- 122 Cities Mortality Reporting System. Vital statistics offices in 122 U.S. cities report pneumonia and influenza (P&I)-related deaths on a weekly basis.
- National Notifiable Disease Surveillance System (NNDSS) pediatric deaths. State health departments report influenza-associated pediatric deaths to CDC.

d) State-level assessments

- State and territorial epidemiologists' reports. Health departments provide weekly reports on the overall level of influenza activity in their states/territories.

It is not possible to provide an absolute case count for influenza or to determine population-based rates of infection or illness on a national level because many infected persons are asymptomatic or experience only mild illness and do not seek medical care. Also, laboratory testing is rare in less severe cases, and testing late in the course of illness (e.g., in cases with severe complications) can yield false-negative results because the patient is no longer shedding virus. Nevertheless, weekly data on outpatient visits for ILI, hospitalizations, and deaths allow CDC to monitor regional disease trends and to compare the timing and intensity of the current season to that of previous seasons.

Influenza surveillance has traditionally been conducted from October through May. In recent years, however, increasing numbers of healthcare providers, laboratories, and health departments have conducted influenza surveillance year-round. This enhancement is an important part of surveillance for novel strains of influenza.

2. Influenza surveillance coordinators

Currently, health departments in all 50 states—as well as in Chicago, New York City, and Washington, DC—have dedicated influenza surveillance coordinators who work at least part-time on influenza surveillance. The roles of the coordinators are to:

- Maintain the current influenza Sentinel Provider Network
- Oversee the surveillance enhancements described below
- Promote year-round influenza surveillance
- Remain in close contact with the CDC Influenza Branch
- Maintain working relationships with the state public health laboratory

C. Surveillance for novel strains of influenza during the Pandemic Alert Period

1. Monitoring for novel strains of influenza

During the Pandemic Alert Period, CDC will issue recommendations for enhanced surveillance to identify patients at increased risk for infection with a novel virus. Novel influenza strains might include avian influenza viruses that can infect humans, other animal influenza viruses (such as swine influenza viruses) that can infect humans, or new or re-emergent human influenza strains that cause cases or clusters of human disease.

The specific recommendations will depend on the epidemiology of the virus and the clinical characteristics of the human cases as they are known at the time, and will most likely focus on severely ill, hospitalized, or ambulatory patients who meet certain epidemiologic and clinical criteria. For example, since February 2004, CDC has recommended enhanced surveillance to identify patients potentially infected with avian influenza A (H5N1). The current recommendations are summarized in Appendix 2.

State and local health departments will be notified of current recommendations via the Health Alert Network (HAN) and Epi-X. Health departments should distribute the recommendations to healthcare providers and will be responsible for receiving initial reports of potential cases in their jurisdictions.

Once a novel strain detected abroad exhibits sustained human-to-human transmission (WHO Phase 6), recommendations for further intensified virologic and disease surveillance will be issued and might include recommendations for stepped-up disease surveillance at U.S. ports of entry (see **Supplement 8**).

2. Reporting novel strains of influenza

- Clinicians should immediately contact the health department when they suspect a human case of infection with an avian or animal strain of influenza or with any other novel human influenza strain. Clinical algorithms for managing patients with possible novel influenza infection are provided in **Supplement 5.**

- State and local health departments should in turn immediately report to CDC any influenza cases that:
  - Test positive for a novel influenza subtype, *or*
  - Meet the enhanced surveillance case definition in effect at that time, *and*
  - Cannot be subtyped in the state public health laboratory because appropriate reagents or biocontainment equipment is not available (see **Supplement 2**).

Reference testing guidelines for potential pandemic strains of influenza are provided in **Supplement 2**.

- Health departments should call the CDC Emergency Response Hotline (770-488-7100) to report a suspected case of infection with avian influenza A (H5N1) or any other novel influenza virus. This number is available 24 hours a day, 7 days a week. Hotline staff will notify a member of the Influenza Branch who will contact the health department to answer questions and provide guidance.
- Following the initial telephone report, health department officials should complete a CDC case screening and report form (obtained from the Hotline or from Epi-X) that includes the CDC case ID number provided during the phone consultation. CDC staff will assist local and state health departments, as needed, in completing the form, which should be faxed to CDC at 888-232-1322 with a cover sheet that says: "ATTN: Influenza case reporting." The case screening and report form used to report suspected cases of human infection with influenza A (H5N1) is provided in Appendix 3.
- If infection with a novel influenza virus is confirmed, states may request CDC assistance with a case investigation to identify the source of infection and determine the course of illness. CDC will assist the state health department in monitoring the close contacts of the ill person.

D. Veterinary surveillance

In the United States, surveillance for avian influenza is conducted by states, the poultry industry, and the U.S. Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS) (Appendix 4). Diagnostic testing is performed by state and industry laboratories, with confirmatory testing by USDA/APHIS Veterinary Services at the National Veterinary Services Laboratories in Ames, Iowa.

CDC and state health departments will continue to assist USDA and state veterinary diagnostic laboratories, as requested, in monitoring influenza strains among poultry and swine. Recent instances of human infection with avian influenza viruses are described in **Supplement 2**, Box 2.

E. Preparedness planning for virologic and disease surveillance during a pandemic

Surveillance enhancements that will be needed during a pandemic should be developed during the Interpandemic and Pandemic Alert Periods so that baseline data for interpreting information gathered during the pandemic will be available and staff will have experience and familiarity with new methodologies.

1. Virologic surveillance

During an influenza pandemic, the volume of requests for laboratory testing is expected to increase dramatically. To meet these demands, laboratories should become proficient in methods that allow efficient testing of large numbers of specimens at a lower biosafety level than BSL 3 with enhancements—which is required for viral culture of avian influenza A (H5N1) viruses. To ensure adequate virologic surveillance during a pandemic, state public health laboratories should:

- Be equipped and trained to use RT-PCR for routine influenza testing and to detect novel influenza viruses by RT-PCR or by viral culture, using proper safety precautions
- Maintain reagents and supplies to allow influenza virus testing year-round

- Develop surge capacity to handle increased testing and reporting during a pandemic
- Assist CDC, if requested, in developing an electronic mechanism for reporting influenza testing and results

CDC is currently working with state and local partners to evaluate the utility and feasibility of reporting patient-level data (including zip code and/or county of residence) through an electronic mechanism other than the Public Health Laboratory Information System (PHLIS). Such a system would allow daily (rather than weekly) reporting during a pandemic and analysis of virus spread at the county or health district level. During a pandemic—as the burden of disease increases and state and local health departments face multiple, competing demands—it might be necessary to adjust surveillance strategies and reassess the need for frequent (or daily) reporting.

2. Outpatient surveillance

Surveillance for outpatient visits for ILI is conducted via the SPN, a collaborative effort among state health departments, healthcare providers, and CDC. State health departments recruit and maintain a local network of healthcare providers who report weekly the total number of patient visits and number of patients with ILI. SPN members may also send specimens from a subset of patients with ILI to the state public health laboratory for diagnostic testing at no cost. CDC develops and maintains reporting materials and systems, serves as a data repository, and provides feedback to the states. Each state should have at least one sentinel provider per 250,000 persons (or a minimum of 10 providers in states with smaller populations) that reports year-round.

CDC is exploring options for enhancing or supplementing ILI outpatient surveillance at the national, regional, and state levels, given that healthcare providers might not be able to report ILI in a timely manner when overwhelmed with patients during an emergency. Existing electronic data sources that might increase the geographic completeness, frequency of reporting, and sustainability of ILI data include:

- BioSense system, which includes ICD-9-coded outpatient visits at DOD ambulatory-care centers and Department of Veterans Affairs outpatient clinics. Studies are underway to determine if BioSense data can be combined with SPN data in a useful way and if they can be reported and analyzed daily.
- Existing emergency department "chief complaint" monitoring systems used by several states. Studies are underway to determine if these data can be added to SPN data and if they can be reported and analyzed daily.

CDC is also working with state and local partners to evaluate the need for and utility and feasibility of expanding SPN to allow analysis of ILI data at the county or health-district level and to provide data that are updated daily rather than weekly. Options for improving the analysis of ILI data include the use of:

- Outbreak detection algorithms that might identify aberrant increases in ILI activity at the individual provider/site level
- Daily analyses of SPN data for use by CDC and state health departments. CDC does not plan to ask sentinel providers to report more than once a week.

Some states are considering the use of systematic phone surveys to supplement SPN data during a pandemic by providing estimates of local cases and affected households. CDC will explore the utility and feasibility of conducting this type of survey on a national level.

3. Hospitalization surveillance

During a pandemic, hospitalization data will be needed on a frequent basis in all parts of the country to monitor disease severity and determine the most severely affected age groups. At present, however, surveillance for hospitalizations associated with influenza is limited to the collection of data on pediatric hospitalizations in 12 large metropolitan areas (see Table 1). In January 2006, the EIP influenza project will be expanded to include laboratory-confirmed influenza-associated hospitalizations of adults as well as children.

CDC is exploring options for expanding hospitalization surveillance to obtain data from all age groups in all parts of the country and obtaining more detailed information from a small number of sites. Some options under review include:

- Continuing to work with the Council of State and Territorial Epidemiologists (CSTE) to make laboratory-confirmed influenza-associated hospitalizations nationally notifiable. A position statement to add influenza infection requiring hospitalization to the list of nationally notifiable diseases was rejected by CSTE members in June 2005 but will be resubmitted in June 2006.
- Obtaining timely hospital discharge data to estimate the number of influenza-associated hospitalizations across the country
- Adding a hospitalization surveillance component to the national BioSense system
- Developing protocols for active population-based hospitalization surveillance, including specimen collection and virologic testing from a subset of hospitalized patients in all age groups in a limited number of sites
- Developing protocols for reporting the number of influenza-associated hospitalizations

4. Mortality surveillance

The collection of mortality data can also help health departments monitor the severity of a pandemic and determine which age groups and areas are most affected. Although pediatric deaths due to laboratory-confirmed influenza are nationally notifiable (as of October 2004), timely data on influenza deaths in other age groups are limited to information provided by the 122 Cities Mortality Reporting System, which provides weekly reports of the total number of death certificates that list P&I as a cause of death and the total number of death certificates filed (Table 1). Although the National Center for Health Statistics (NCHS) also collects mortality data, these data are not available until 2-3 years after each influenza season.

During a pandemic, state and local policy-makers and public health officials will likely ask health departments to provide mortality data to guide decision-making on control and response measures. In addition, CDC will request mortality data from each state to help guide national response measures. To help ensure uniform data collection across jurisdictions, CDC will provide case definitions and reporting procedures via HAN and Epi-X.

CDC is also investigating the feasibility of obtaining mortality data through the Electronic Death Registration (EDR) Project (http://www.naphsis.org/projects/index.asp?bid=374) and the validity of estimating national mortality based on data from the 122 Cities Mortality Reporting System. State-specific mortality cannot be estimated from data provided by the 122 Cities system.

5. State influenza activity assessments

During the Interpandemic Period, state health departments provide weekly assessments of the overall level of influenza activity (i.e., none, sporadic, local, regional, widespread) in the state. These assessments are used to compare the extent of influenza activity from state to state, and are the only state-level influenza surveillance data that CDC makes publicly available during interpandemic influenza seasons. The state influenza activity assessments are used to generate the influenza activity map, which is the most frequently referenced component of national influenza surveillance (see www.cdc.gov/flu/weekly/usmap.htm). During a pandemic, CDC will recommend that these assessments be made year-round, rather than only October through May.

S1-IV. RECOMMENDATIONS FOR THE PANDEMIC PERIOD

During a pandemic, more detailed information on age-specific, population-based rates of severe disease and patient outcomes will be needed than can be provided through routine national surveillance. This information will be obtained through enhanced national surveillance and carefully designed studies in a limited number of sites. These data will provide information to guide response and policy development during a pandemic. Outbreak investigations and special studies are described in Part 1.

A. Enhanced surveillance

During an influenza pandemic, CDC will use data from the U.S. collaborating laboratories of the WHO Global Influenza Surveillance Network and the NREVSS to detect the introduction and early cases of a pandemic influenza virus in the United States, track the virus' introduction into local areas, and monitor changes in the pandemic virus, including development of antiviral resistance. States should conduct the following activities:

- Distribute to healthcare providers the current CDC recommendations for enhanced surveillance for the detection of the first cases of the pandemic virus in their jurisdictions.
- Facilitate the collection and testing of appropriate specimens as recommended for early detection of pandemic virus at the local level.
- Increase testing and the frequency of reporting of virologic data. The most intense testing will be necessary during the early stages of a pandemic, when detecting the introduction of the virus into a state or community is the primary goal.
- Once the virus has been identified throughout the state, the level of testing can be decreased to a level more like that of a non-pandemic influenza season. State health officials can determine the level of testing for their jurisdictions.
- As part of the effort to monitor antigenic and genetic changes and changes in antiviral resistance patterns in the pandemic virus, state public health laboratories should forward a subset of virus isolates to CDC. CDC will advise states on the number of and clinical criteria for these isolates. **Supplement 2** contains additional information on monitoring for antiviral resistance.

During an influenza pandemic, CDC will use data from SPN, hospitalization surveillance, state and territorial epidemiologists' assessments, the 122 Cities Mortality Reporting System, NNDSS, and other data systems to:

- Monitor the pandemic's impact on health
- Track trends in influenza disease activity and identify populations that are severely affected
- Serve as an early warning system to detect increases in ILI in the community

State health departments should:

- Communicate to all partners the heightened need for timely and complete surveillance data.
- Ensure that all sentinel provider surveillance sites are reporting weekly, regardless of the time of year.
- Ensure that EIP and NVSN hospitalization surveillance is active.
- Report state influenza activity level in a timely manner.
- Facilitate timely reporting of 122 Cities Mortality Reports and pediatric deaths.
- Implement state and local collection of influenza-associated mortality data and reporting of statewide mortality data to CDC, following CDC guidelines for uniform data collection and reporting.

B. Scaled-back surveillance

Enhanced surveillance will be conducted during the introduction, initial spread, and first waves of a pandemic. Over time, as more persons are exposed, the pandemic strain is likely to become a routinely circulating influenza A subtype. When that happens, the activities of the national influenza surveillance system will revert to the frequency and intensity typically seen during interpandemic influenza seasons. The return to interpandemic surveillance will occur as soon as feasible, and the change will be communicated to all surveillance partners.

TABLE 1. COMPONENTS OF THE NATIONAL INFLUENZA SURVEILLANCE SYSTEM

Activity	Surveillance type	Description
U.S. collaborating laboratories of the: • WHO Global Influenza Surveillance Network • National Respiratory and Enteric Virus Surveillance System (NREVSS)	Virologic surveillance	Collaborating laboratories report weekly to CDC the number of influenza tests performed and the number of positive results by type, and in some cases, subtype and age group. If non-subtypable viruses or unusual subtypes are detected, the specimens are sent to the state public health laboratory or to CDC for further testing.
Sentinel Provider Network (SPN)	Outpatient surveillance	Approximately 2,300 healthcare providers monitor outpatient visits for ILI (fever >100°F or 37.8°C AND sore throat and/or cough in the absence of a known cause other than influenza). Specimens from a small subset of patients are submitted to state public health laboratories for influenza virus testing.
Emerging Infections Program (EIP) influenza project	Hospital surveillance	Eleven EIP sites report to CDC cases of laboratory-confirmed influenza-related hospitalizations in children aged <18 years on a bi-weekly basis.
New Vaccine Surveillance Network (NVSN) pediatric hospitalizations	Hospital surveillance	NVSN enrolls a subset of patients aged <5 years who are hospitalized with fever or respiratory symptoms. Nose and throat swabs are obtained and tested for influenza by viral culture and RT-PCR. The rate of laboratory-confirmed influenza-related hospitalizations is reported to CDC on a bi-weekly basis.
122 Cities Mortality Reporting System	Mortality surveillance	Municipal vital records offices transmit weekly data to CDC on the total number of death certificates filed and the number with pneumonia and/or influenza listed as a cause of death.
National Notifiable Disease Surveillance System (NNDSS) influenza-associated pediatric mortality	Mortality surveillance	Participating state health departments report to CDC all laboratory-confirmed influenza-related deaths among children <18 years.
State and territorial epidemiologists' reports	State-level assessments	Health departments report on a weekly basis the overall level of influenza activity as none, sporadic, local, regional, or widespread.

APPENDIX 1. TYPES OF INFLUENZA SURVEILLANCE

A. Virologic surveillance

- A network of ~75 WHO collaborating laboratories and ~90 NREVSS collaborating laboratories report the total number of respiratory specimens tested and the number positive for influenza by type, subtype, and age group to CDC each week. (Because ~40 of the NREVSS laboratories are also WHO laboratories, the total number in the WHO/NREVSS network is ~125.) Data from the two networks are combined and analyzed together.
- WHO collaborating laboratory network
  - All 50 state health department laboratories, 4 large county public health laboratories, a DOD reference laboratory, and ~25 tertiary-care hospital and academic center laboratories participate.
  - State and county public health laboratories subtype (i.e., A/H1 vs. A/H3) ~80% of their influenza A isolates.
  - Laboratories report the number of tests performed and results by age group to CDC's Influenza Branch.
  - Approximately 30% of laboratories report specimen-level data electronically using PHLIS, ~40% report aggregate weekly data via the Internet, and ~30% report aggregate weekly data via fax.
- NREVSS collaborating laboratory network
  - Primarily hospital laboratories
  - Most do not subtype influenza viruses, and none report age-group data
  - Laboratories report aggregate weekly numbers of tests performed and results to CDC's Respiratory and Enteric Viruses Branch (REVB) by phone or Internet.
- Laboratories test for influenza viruses by viral culture, PCR, or antigen detection.
- Most laboratories maintain the ability to test for influenza year-round.
- Data are available to state health department influenza surveillance coordinators on a password-protected website that is updated once a week during October through May and periodically throughout the summer. National and regional data are made available to all states, and state-specific data (including a laboratory-specific line list) are available to the states from which the data were reported.

B. Outpatient ILI surveillance (Sentinel Provider Network)

- Network of ~2,300 primary-care providers in all 50 states record the number of outpatients seen for any reason and the number with ILI by age group and report directly to CDC each week.
- ILI is defined as fever (>100°F or 37.8°C) AND sore throat and/or cough in the absence of a known cause other than influenza.
- All providers report from October through May, and approximately one third of the regular reporters report year-round.
- The network is a collaborative effort between CDC and state health departments.
  - State health department influenza surveillance coordinators recruit and maintain a network of providers and arrange for testing, free of charge, for a subset of specimens from providers.
  - CDC develops and maintains reporting materials and systems, serves as a data repository, and provides data feedback to the states.
- Providers collect two or three specimens from patients with ILI at the beginning, middle, and end of the season and from any unusual clinical cases, severe cases, outbreak-related cases, and patients with ILI during the summer.
- Providers report to CDC via a password-protected Internet site (75%), fax (13%), or phone (12%).

- Data are available to state health department influenza surveillance coordinators on a password-protected website. Data reported by providers on the Internet are available in real time, and data reported to CDC by fax are updated once each weekday. Regional data are available to all states, whereas state-specific data are available to the states from which the data were reported.

C. Hospitalization surveillance

- Hospitalizations associated with laboratory-confirmed influenza in children are monitored in 12 metropolitan areas through two surveillance networks that report patient-level data to CDC every 2 weeks.
  - Emerging Infections Program (EIP) influenza project. Children aged <18 years are monitored in 11 metropolitan areas from October 1 through April 30; laboratory testing is part of routine patient care. The EIP influenza project will expand to include all age groups in January 2006.
  - New Vaccine Surveillance Network (NVSN). A sample of children aged <5 years is monitored in three metropolitan areas (two are EIP influenza project sites) from October 1 through March/April; all sampled children with fever and respiratory symptoms are tested on admission.

D. Mortality surveillance

- Vital statistics offices in 122 cities covering between one-fourth and one-third of the U.S. population report weekly throughout the year the total number of death certificates filed and the number with pneumonia and/or influenza listed anywhere on the death certificate, by age group. No additional information (e.g., underlying medical condition, demographics) is available. On average, there is a 15-day lag from death to report to CDC.
- Weekly mortality data from the 122 cities are compared to a seasonal baseline calculated using a robust regression procedure run on the previous 5 years of data. If the proportion of P&I deaths for a given week exceeds the baseline value for that week by a statistically significant amount, P&I deaths are said to be above the epidemic threshold, and the proportion of deaths above threshold are considered attributable to influenza.
  - Data from all 122 cities are combined, and the percentage of all P&I deaths are calculated and compared to the expected percentage for that week.
  - Data can be analyzed by age group and geographic region, but interpretation of the data requires the development of a separate baseline for each data subset. It is not valid to compare data from a particular city or region to the national baseline.
- Detailed data (e.g., person-level data including multiple causes of death, underlying medical conditions, demographics) on ~99% of deaths in the United States are available from NCHS, but these data have a time lag of ~2-3 years.
- Pediatric deaths associated with laboratory-confirmed influenza were made nationally notifiable in October 2004. During the 2004-2005 season, the condition was reportable in 13 states; many others instituted voluntary reporting until the legal requirement was passed. CDC receives electronic, patient-level data on these deaths. The timeliness of these data cannot yet be assessed.

E. State-level influenza activity assessments

State health departments report a weekly assessment of the overall level of influenza activity (none, sporadic, local, regional, or widespread) in the state (see box below). These assessments are used to compare the extent of influenza activity from state to state and represent the only state-level influenza surveillance data that CDC makes publicly available during the interpandemic influenza season.

TABLE 2. COMPONENTS OF THE NATIONAL INFLUENZA SURVEILLANCE SYSTEM

Activity level	ILI activity*/outbreaks		Laboratory data
No activity	Low	**and**	No lab-confirmed cases†
Sporadic	Not increased	**and**	Isolated lab-confirmed cases
	or		Lab-confirmed outbreak in one institution‡
Local	Not increased		Recent (within the past 3 weeks) lab evidence of influenza in region with increased ILI
Regional (doesn't apply to states with ≤4 regions)	Increased ILI in 1 region**; ILI activity in other regions is not increased	**and**	Recent (within the past 3 weeks) lab evidence of influenza in region with the outbreaks; virus activity is no greater than sporadic in other regions
	or		
	2 or more institutional outbreaks (ILI or lab confirmed) in 1 region; ILI activity in other regions is not increased		Recent (within the past 3 weeks) lab-confirmed influenza in the affected regions
Widespread	Increased ILI in ≥2 but less than half of the regions	**and**	Recent (within the past 3 weeks) lab-confirmed influenza in the affected regions
	or		
	Institutional outbreaks (ILI or lab confirmed) in ≥2 and less than half of the regions	**and**	Recent (within the past 3 weeks) lab-confirmed influenza in the state.
	Increased ILI and/or institutional outbreaks (ILI or lab confirmed) in at least half of the regions		

* ILI activity can be assessed using a variety of data sources, including Sentinel providers, school/workplace absenteeism, and other syndromic surveillance systems that monitor influenza-like illness.

† Lab-confirmed case = case confirmed by rapid diagnostic test, antigen detection, culture, or PCR. Care should be given when relying on results of point-of-care rapid diagnostic test kits during times when influenza is not circulating widely. The sensitivity and specificity of these tests vary, and the predicative value positive may be low outside of peak influenza activity. Therefore, a state may wish to obtain laboratory confirmation of influenza by testing methods other than point-of-care rapid tests for reporting the first laboratory-confirmed case of influenza of the season.

‡ Institution = nursing home, hospital, prison, school, etc.

** Region = population under surveillance in a defined geographical subdivision of a state. A region could be comprised of one or more counties and would be based on each state's specific circumstances. Depending on the size of the state, the number of regions could range from 2 to approximately 12. The definition of regions would be left to the state, but existing state health districts could be used in many states. Allowing states to define regions would avoid somewhat arbitrary county lines and allow states to establish divisions that make sense based on geographic population clusters. Focusing on regions larger than counties would also improve the likelihood that data needed for estimating activity would be available.

APPENDIX 2. INTERIM RECOMMENDATIONS: ENHANCED U.S. SURVEILLANCE AND DIAGNOSTIC EVALUATION TO IDENTIFY CASES OF HUMAN INFECTION WITH AVIAN INFLUENZA A (H5N1)

NOTE: This guidance pertains to the avian influenza A (H5N1) circulating as of October 2005 CDC will provide updated guidance for avian influenza A (H5N1) or for new situations, as needed, through the Health Alert Network.

Enhanced surveillance efforts by state and local health departments, hospitals, and clinicians are needed to identify patients at increased risk for influenza A (H5N1). Interim recommendations are as follows:

- Testing for avian influenza A (H5N1) is indicated for **hospitalized** patients with:
  - Radiographically confirmed pneumonia, acute respiratory distress syndrome (ARDS), or other severe respiratory illness for which an alternative diagnosis has not been established, **and**
  - History of travel within 10 days of symptom onset to a country with documented avian influenza A (H5N1) infections in poultry and/or humans. (For a regularly updated listing of H5N1-affected countries, see the World Organization for Animal Health [OIE] website at http://www.oie.int/eng/en_index.htm and the WHO website at http://www.who.int/en/).

OR

- Testing for avian influenza A (H5N1) should be considered on a case-by-case basis in consultation with state and local health departments for **hospitalized or ambulatory** patients with:
  - Documented temperature of >100.4°F (>38°C); **and**
  - One or more of the following: cough, sore throat, or shortness of breath; **and**
  - History of contact with poultry (e.g., visited a poultry farm, a household raising poultry, or a bird market) or a known or suspected human case of influenza A (H5N1) in an H5N1-affected country within 10 days prior to onset of symptoms.

APPENDIX 3. CDC HUMAN INFLUENZA A(H5) CASE SCREENING AND REPORT FORM

Human Influenza A (H5)

Human Influenza A (H5) Domestic Case Screening Form

CDC Case ID:

1. Reported By

Date reported to state or local health department: __ __ / __ __ / __ __ __ __ (m m d d y y y y)	State/ local Assigned Case ID:
Last Name:	First Name:
State:	Affiliation:	Email:
Phone 1:	Phone 2:	Fax:

2. Patient Information

City of Residence: County: State:

Age at onset: _____ ☐ Year(s) ☐ Month(s)

Race: *(Choose One)*
☐ American Indian/Alaska Native ☐ White
☐ Asian ☐ Unknown
☐ Black
☐ Native Hawaiian/Other Pacific Islander

Sex: ☐ Male ☐ Female

Ethnicity: ☐ Non Hispanic ☐ Hispanic

3. Optional Patient Information

Last Name: First Name:

4. Signs and Symptoms

A. Date of symptom onset: __ __ / __ __ / __ __ __ __ (m m d d y y y y)

B. What symptoms and signs did the patient have during the course of illness? (check all that apply)

☐ Fever > 38° C (100.4° F) ☐ Feverish (temperature not taken) ☐ Conjunctivitis

☐ Cough ☐ Headache ☐ Shortness of breath

☐ Sore throat ☐ Other (specify): _____

C. Was a chest X-ray or chest CAT scan performed? ☐ Yes* ☐ No ☐ Unknown

If yes*, did the patient have radiographic evidence of pneumonia or respiratory distress syndrome (RDS)? ☐ Yes* ☐ No ☐ Unknown

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION
SAFER • HEALTHIER • PEOPLE™

Epidemiologic Risk Factors

CDC Case ID:

5. Travel/Exposures

A. In the 10 days prior to illness onset, did the patient travel to any of the countries listed in the table below? If yes*, please fill in arrival and departure dates for all countries that apply. ☐ Yes* ☐ No** ☐ Unknown

****If patient did not travel outside U.S., skip to question 6.**

Country	Arrival Date	Departure Date	Country	Arrival Date	Departure Date
☐ Afghanistan			☐ Myanmar (Burma)		
☐ Bangladesh			☐ Nepal		
☐ Brunei			☐ North Korea		
☐ Cambodia			☐ Oman		
☐ China			☐ Pakistan		
☐ Hong Kong			☐ Papua New Guinea		
☐ India			☐ Philippines		
☐ Indonesia			☐ Saudi Arabia		
☐ Iran			☐ Singapore		
☐ Iraq			☐ South Korea		
☐ Israel			☐ Syria		
☐ Japan			☐ Taiwan		
☐ Jordan			☐ Thailand		
☐ Laos			☐ Turkey		
☐ Lebanon			☐ Viet Nam		
☐ Macao			☐ Yemen		
☐ Malaysia					

For the questions 5B to 5E,
In the 10 days prior to illness onset, <u>while in the countries</u> listed above . . . .

B. Did the patient come within 1 meter (3 feet) of any live poultry or domesticated birds (e.g. visited a poultry farm, a household raising poultry, or a bird market)? ☐ Yes* ☐ No ☐ Unknown

If Yes*

C. Did patient touch any recently butchered poultry? ☐ Yes ☐ No ☐ Unknown

D. Did the patient visit or stay in the same household with anyone with pneumonia or severe flu-like illness? ☐ Yes ☐ No ☐ Unknown

E. Did the patient visit or stay in the same household with a suspected human influenza A(H5) case?* ☐ Yes ☐ No ☐ Unknown

F. Did the patient visit or stay in the same household with a known human influenza A(H5) case?* ☐ Yes ☐ No ☐ Unknown

** SEE Influenza A (H5): Interim U.S. Case Definitions*

(continued from previous page)

CDC ID:

6. Exposure for Non Travelers	
For patients whom did not travel outside the U.S., **in the 10 days prior to illness onset**, did the patient visit or stay in the same household with a traveler returning from one of the countries listed above who developed pneumonia or severe flu-like illness?	☐ Yes* ☐ No ☐ Unknown
If yes*, was the contact a confirmed or suspected H5 case patient?	☐ Yes* ☐ No ☐ Unknown
If yes*: CDC ID: _____ STATE ID: _____	

Laboratory Evaluation

7. State and local level influenza test results	
Specimen 1	
☐ NP swab ☐ Broncheoalveolar lavage specimen (BAL) ☐ NP aspirate ☐ OP swab ☐ Other _____	Date Collected: __ __ / __ __ / __ __ __ __ m m d d y y y y
Test Type: ☐ RT-PCR ☐ Direct fluorescent antibody (DFA) ☐ Viral Culture ☐ Rapid Antigen Test* *Name of Rapid Test:	Result: ☐ Influenza A ☐ Influenza B ☐ Influenza (type unk) ☐ Negative ☐ Pending
Specimen 2	
☐ NP swab ☐ Broncheoalveolar lavage specimen (BAL) ☐ NP aspirate ☐ OP swab ☐ Other _____	Date Collected: __ __ / __ __ / __ __ __ __ m m d d y y y y
Test Type: ☐ RT-PCR ☐ Direct fluorescent antibody (DFA) ☐ Viral Culture ☐ Rapid Antigen Test* *Name of Rapid Test:	Result: ☐ Influenza A ☐ Influenza B ☐ Influenza (type unk) ☐ Negative ☐ Pending
Specimen 3	
☐ NP swab ☐ Broncheoalveolar lavage specimen (BAL) ☐ NP aspirate ☐ OP swab ☐ Other _____	Date Collected: __ __ / __ __ / __ __ __ __ m m d d y y y y
Test Type: ☐ RT-PCR ☐ Direct fluorescent antibody (DFA) ☐ Viral Culture ☐ Rapid Antigen Test* *Name of Rapid Test:	Result: ☐ Influenza A ☐ Influenza B ☐ Influenza (type unk) ☐ Negative ☐ Pending

(continued from previous page)

CDC ID:

8. List specimens sent to the CDC

Select a SOURCE* from the following list for each specimen: Serum (acute), serum (convalescent), NP swab, NP aspirate, broncheoalveolar lavage specimen (BAL), OP swab, tracheal aspirate, or tissue

Specimen 1: ☐ Clinical Material ☐ Extracted RNA ☐ Virus Isolate	Source*: ----------	Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y) Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)
Specimen 2: ☐ Clinical Material ☐ Extracted RNA ☐ Virus Isolate	Source*: ----------	Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y) Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)
Specimen 3: ☐ Clinical Material ☐ Extracted RNA ☐ Virus Isolate	Source*: ----------	Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y) Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)
Specimen 4: ☐ Clinical Material ☐ Extracted RNA ☐ Virus Isolate	Source*: ----------	Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y) Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)
Specimen 5: ☐ Clinical Material ☐ Extracted RNA ☐ Virus Isolate	Source*: ----------	Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y) Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)
Carrier:	Tracking #:	

9. Case Notes:

(continued from previous page)

CDC ID:

CDC Contact Information (FOR CDC USE ONLY)	
Case status and date status applied: ☐ Clinical Case (lab results pending) __ __ / __ __ / __ __ __ __ (m m d d y y y y) ☐ Influenza A pos. Case (subtype pending) __ __ / __ __ / __ __ __ __ (m m d d y y y y) ☐ Confirmed Case __ __ / __ __ / __ __ __ __ (m m d d y y y y)	☐ Ruled Out/Non-Case: __ __ / __ __ / __ __ __ __ (m m d d y y y y) Reason: ☐ Influenza A neg. (by PCR, viral culture, or influenza A serology) ☐ Non-H5 Influenza Strain ☐ Other etiology* ☐ Did not meet case definition
Date Entered by CDC: __ __ / __ __ / __ __ __ __ (m m d d y y y y)	Contact Date: __ __ / __ __ / __ __ __ __ (m m d d y y y y)
Name of CDC Contact:	

*Alternative Diagnosis			
A. Was an alternative non-influenza respiratory pathogen detected? If yes* specify:	☐ Yes*	☐ No	☐ Unknown
B. Was there a diagnosis other than respiratory infection? If yes* specify:	☐ Yes*	☐ No	☐ Unknown

supplement 2
laboratory diagnostics
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SUMMARY OF ROLES AND RESPONSIBILITIES FOR PUBLIC HEALTH AND CLINICAL LABORATORIES IN LABORATORY DIAGNOSTICS

INTERPANDEMIC AND PANDEMIC ALERT PERIODS

Clinical and hospital laboratories:

- Work with state and local health departments to address laboratory surge capacity issues and train personnel in management of respiratory specimens during an influenza pandemic.
- Send clearly labeled specimens from patients with suspected novel influenza to state or local health departments. Hospital labs should NOT attempt to isolate influenza viruses from patients with suspected novel influenza virus infection.
- Institute surveillance for influenza-like illnesses (ILI) among laboratory personnel working with novel influenza viruses.

State and local public health laboratories:

- Work with federal partners to enhance laboratory-based monitoring of seasonal influenza virus subtypes, as described in **Supplement 1**.
- Conduct testing for novel subtypes of influenza viruses only if BSL-3 biocontainment conditions with enhancements are available.
- Institute surveillance for ILI among laboratory personnel.
- Conduct preparedness planning to support the response to an influenza pandemic.

HHS responsibilities:

- Monitor preparedness and laboratory capacity for seasonal influenza and assess surge capacity.
- Provide technical support to the WHO Influenza Network and ministries of health and agriculture, as requested, in analyzing novel influenza virus subtypes—including avian isolates and human isolates with pandemic potential—in terms of antigenicity, RNA sequence, and drug sensitivities.
- Work with state and local public health laboratories to ensure that diagnostics for identifying "pandemic alert" strains are available and are used safely and effectively.
- Provide guidance on biosafety and safe handling of respiratory specimens from potential cases of pandemic influenza.

PANDEMIC PERIOD

Clinical and hospital laboratories:

- Scale up to manage increased numbers of requests for influenza testing.
- Send selected specimens from possible pandemic influenza patients to state or local health departments.

State and local public health laboratories:

- Scale up to manage increased numbers of requests for influenza testing.
- Work with federal partners to provide healthcare providers and clinical laboratories with guidelines on all aspects of specimen management and diagnostic testing.

- Work with federal partners to monitor the pandemic virus and conduct special studies related to vaccine development, or other aspects of the response.

HHS responsibilities:

- Work with U.S. and global partners to characterize new pandemic viruses in terms of antigenicity, RNA sequence, and drug sensitivities, and to monitor changes over time.
- Work with state and local public health laboratories to ensure the availability and the safe and effective use of diagnostic tests and reagents.
- Conduct reference testing of positive samples, and perform viral isolation, especially at the beginning of a pandemic.
- Provide laboratory support for the selection of seed strains to be used in a vaccine against the pandemic virus.

S2-I. RATIONALE

The goals of diagnostic testing during a pandemic are to:

- Identify the earliest U.S. cases of pandemic influenza (whether the pandemic begins in the United States or elsewhere).
- Support disease surveillance to monitor the pandemic's geographic spread and impact of interventions.
- Facilitate clinical treatment by distinguishing patients with influenza from those with other respiratory illnesses.
- Monitor circulating viruses for antiviral resistance.

Diagnostic testing for pandemic influenza virus may involve a range of laboratory assays, including rapid antigen tests, reverse-transcription polymerase chain reaction (RT-PCR), virus isolation, and immunofluorescence antibody (IFA) assays (see Box 1 and Appendix 1).

During the earliest stages of a pandemic, public health, hospital, and clinical laboratories might receive a large and potentially overwhelming volume of clinical specimens. Pre-pandemic planning is therefore essential to ensure the timeliness of diagnostic testing and the availability of diagnostic supplies and reagents, address staffing issues, and disseminate protocols for safe handling and shipping of specimens. Once a pandemic is underway, the need for laboratory confirmation of clinical diagnoses may decrease as the virus becomes widespread.

S2-II. OVERVIEW

Supplement 2 provides recommendations to state and local public health partners and other laboratories on the use of diagnostic tests to detect, characterize, and monitor novel subtypes of influenza, including avian influenza A (H5N1) and other viruses with pandemic potential. The recommendations for the Interpandemic and Pandemic Alert Periods focus on laboratory testing in support of seasonal influenza surveillance, laboratory-based detection of novel influenza subtypes, and preparedness planning to support the laboratory component of the response to a pandemic (e.g., detection and characterization of viruses, case reporting, specimen management, surge capacity). The recommendations for the Pandemic Period focus on the provision of laboratory support for disease surveillance and to assist clinicians and hospitals. The recommendations also cover occupational health issues for laboratory workers.

S2-III. RECOMMENDATIONS FOR THE INTERPANDEMIC AND PANDEMIC ALERT PERIODS

A. Laboratory support for seasonal influenza surveillance

State and local public health laboratories and clinical laboratories (including hospital and private commercial laboratories) should continue to participate in laboratory-based surveillance for new subtypes of influenza through the U.S.-based laboratories in the World Health Organization (WHO) Global Influenza Surveillance Network and the National Respiratory and Enteric Virus Surveillance System (NREVSS). Additional information on seasonal influenza surveillance (including surveillance for influenza mortality and pediatric hospitalizations) is provided in **Supplement 1**. Information on the WHO Global Influenza Surveillance Network and NREVSS is provided in Box 2.

B. Laboratory testing for novel influenza subtypes

During the Pandemic Alert Period, state and local health departments, hospitals, and clinicians should enhance surveillance to identify patients who may present with possible cases of novel influenza (see Appendix 2). Health Alert Network (HAN) messages will be issued, as needed, to provide updates and guidance as new situations arise.

State and local public health laboratories should be prepared to process and, in some instances, test—if they have the capability (see below)—specimens from suspected cases of infection with:

- Avian influenza A (H5N1) and other avian influenza viruses
- Other animal influenza viruses (e.g., swine influenza viruses)
- New or re-emergent human influenza viruses (e.g., H2) with pandemic potential

Clinicians should contact their state or local health departments if they suspect a human case of infection with any novel influenza A virus. State and local health departments, in turn, should contact CDC via the CDC Emergency Response Hotline: 770-488-7100.

Guidelines on when to send specimens or isolates of suspected novel avian or human strains to CDC for reference testing are provided in Appendix 3.

1. Testing for human cases of avian influenza

Currently, avian influenza strains implicated in human disease (in addition to influenza A [H5N1]) include the highly pathogenic avian influenza (HPAI) strain H7N7 and the low pathogenic avian influenza (LPAI) strains H9N2, H7N2, and H7N3 (see Box 3). As of October 2005, no laboratory-confirmed cases of human infection with influenza A (H5N1) had been reported in the United States. However, CDC has confirmed two non-fatal cases of avian A (H7N2) influenza in Virginia and New York (Box 3). As new U.S. cases of human infection with avian influenza viruses are reported, they will be posted at: www.aphis.usda.gov/vs/birdbiosecurity/hpai.html and at: www.cdc.gov/flu.

Recommendations on laboratory testing for human cases of avian influenza are as follows:

- State public health laboratories may conduct testing to identify suspected subtypes of avian influenza, including H5 and H7, if appropriate laboratory capacity and biocontainment equipment are available. Because of the danger that HPAI strains present to the U.S. agricultural industry, U.S. Department of Agriculture (USDA) regulations require that HPAI strains such as H5N1 (which are classified as select agents) must be cultured using BSL-3 biocontainment conditions with enhancements (see Appendix 4).

- Public health laboratories that lack BSL-3 facilities may use RT-PCR with BSL-2 containment to test clinical specimens from suspected human cases of avian influenza to identify and subtype influenza A viruses (e.g., H1, H3, H5, and H7; see S2-III.C). Or, they may send specimens to CDC, using the collection, handling, and shipping procedures described in Appendix 5.

During the Pandemic Alert Period, specimens from suspected cases of human infection with novel influenza viruses should be sent for testing to public health laboratories with proper biocontainment facilities:

- RT-PCR – BSL-2
- Virus isolation – BSL-3 with enhancements

The American Society for Microbiology maintains a list of emergency contacts in state public health laboratories, which is available at: www.asm.org/ASM/files/0000000527/labemergencycontacts[1].pdf.

If an avian influenza strain—or a human virus variant that evolves from it—causes an influenza pandemic, it might become necessary to re-evaluate biocontainment requirements and select agent registration requirements for laboratory testing. CDC and the Laboratory Response Network (LRN) will assist USDA, as requested, in making such a decision.

2. Testing for human influenza strains with pandemic potential

During the Pandemic Alert Period, diagnostic laboratories should be on the alert for new human subtypes of influenza that might have pandemic potential. Recommendations are as follows:

- State and local public health laboratories that can detect human and avian influenza subtypes by RT-PCR should report all unusual subtypes to CDC via the Emergency Response Hotline (770-488-7100).
- Public health laboratories that can detect human (but not avian) influenza subtypes by IFA staining or RT-PCR should send influenza A isolates that cannot be subtyped to CDC. (If an avian strain is suspected, virus isolation and IFA should be performed under BSL-3 conditions with enhancements.)
- Public health laboratories should send specimens to CDC if a patient meets the clinical and epidemiologic criteria for infection with a novel influenza virus and:
  - Tests positive for influenza A by RT-PCR or by rapid diagnostic testing, *or*
  - Tests negative for influenza A by rapid diagnostic testing and/or RT-PCR testing for influenza is not available
- Clinical laboratories that receive diagnostic specimens from patients with suspected novel influenza (based on clinical and epidemiologic data) should contact their state or local health departments.
- If new or re-emergent human influenza strains with pandemic potential are suspected, laboratories should conduct RT-PCR only under BSL-2 containment conditions and viral culture only under BSL-3 conditions with enhancements (see Appendix 4).

C. Laboratory planning to support the response to an influenza pandemic

Advance planning is essential to anticipate adequate laboratory capacity to support medical and public health partners during an influenza pandemic. Some aspects of this planning, such as surge capacity planning, can be coordinated with bioterrorism preparedness planning.

1. Detection and characterization of novel influenza strains

- As of October 2005, about 48 state and large local public health laboratories have received training in RT-PCR protocols for molecular detection of H1, H3, H5, and H7 subtypes. These laboratories should incorporate RT-PCR testing into their standard influenza laboratory activities. Real-time RT-PCR protocols are available through the website of the Association of Public Health Laboratories (APHL) and will be updated as required to monitor the appearance and evolution of novel influenza viruses. A positive RT-PCR test result for a novel influenza strain should be considered presumptive, pending testing by a second reference laboratory.
- State and local public health laboratories should provide hospitals and healthcare providers with information on how to contact the laboratory when a novel influenza subtype is suspected and how to handle, label, and ship clinical specimens for diagnostic evaluation.
- State and local public health laboratories should contact laboratories in their jurisdictions that conduct RT-PCR influenza testing or that have BSL-3 containment facilities to remind them to notify the state health department if they receive specimens from suspected cases of novel influenza.

2. Laboratory reporting

State and local health departments that report laboratory-confirmed seasonal influenza cases to CDC use a variety of reporting mechanisms, including faxes, the Public Health Information System (PHLIS), and a web-based NREVSS data-entry system. Cases of novel influenza should be reported to CDC by the same mechanisms.

3. Distribution of diagnostics reagents and test information

CDC is working with USDA and the Food and Drug Administration (FDA) to address any regulatory barriers to emergency distribution and use of diagnostic tests and reagents during a pandemic. CDC will provide updated preparedness information regarding diagnostic tests and reagents to state and local public health partners via the LRN and HAN.

4. Laboratory surge capacity planning

Health departments should assess projected statewide needs for scaled-up diagnostic activity during the early stages of a pandemic, in terms of laboratory staffing, training, reporting, and supplies, and should develop strategies to address them.

a) Staffing and training

Laboratories should plan for increased staffing needs. Some strategies include:

- Cross-training personnel during the regular influenza season in the use of rapid diagnostic tests and RT-PCR protocols and in reporting results through existing surveillance systems
- Arranging to recruit and train temporary staff for employment during a pandemic

b) Supplies and equipment

Laboratories are likely to require additional diagnostic supplies and equipment to process large numbers of samples during the initial stages of a pandemic. Some preparedness strategies include:

- Establishing the current level of diagnostic supplies, including personal protective equipment for laboratorians (e.g., gloves, masks)
- Assessing anticipated equipment and supply needs, and determining a trigger point for ordering extra resources. Laboratories should also consider the need for back-up sources of supplies if most laboratories in a state or large city rely on the same manufacturer for particular supplies or equipment.
- Determining how consumption of supplies will be tracked during a pandemic

c) Specimen management

State and local health departments should inform and educate public health staff (including laboratorians), local physicians, and hospital workers on safe and effective methods for specimen collection and management, making use of the guidelines in Appendix 5, Guidelines for Collecting and Shipping Specimens for Influenza Diagnostics. Safety issues related to specimen handling are also addressed in **Supplement 4**.

Procedures for specimen collection, handling, and shipping during a pandemic will be the same as those used for seasonal disease surveillance. However, laboratory staff should anticipate shipping a much larger number of specimens in a very short time, especially during the early stages of a pandemic. Once the pandemic is underway and healthcare providers rely on clinical criteria and rapid test kits, more diagnostic activities may be conducted locally and fewer shipments may be needed.

5. Partnerships with healthcare providers and clinical laboratories

Good working relationships between healthcare providers and public health laboratories will facilitate diagnostic activities during a pandemic.

- Public health laboratories should continue to build partnerships with healthcare providers in their jurisdictions, including physicians who participate in the Sentinel Provider Network (SPN) during the regular influenza season (see **Supplement 1**).
- Public health laboratories should build partnerships with clinical laboratories and provide them with updated information and (if feasible) training in influenza diagnostics.

S2-IV. RECOMMENDATIONS FOR THE PANDEMIC PERIOD

A. Laboratory support for disease surveillance

- Public health, hospital, and clinical laboratories will support surveillance for pandemic influenza through the same mechanisms that support laboratory-based surveillance for seasonal influenza. CDC and the LRN will work with state and local health departments to make diagnostic testing for the pandemic virus readily available, both at CDC and at state and local public health laboratories that have implemented RT-PCR protocols.
- As soon as a pandemic strain has been identified, CDC's Influenza Laboratory will develop, produce, and disseminate RT-PCR and IFA reagents, as needed. As necessary, CDC and APHL will also update the RT-PCR protocol currently available to public health laboratories through the APHL website.
- As the pandemic continues, CDC will advise states on when confirmatory testing (i.e., subtyping) is required. Although confirmatory testing will be required when the pandemic begins, the level of testing will decrease as the virus becomes widespread.
- CDC will advise states on the percentage of isolates per week or month that they should send to CDC as part of efforts to monitor changes in the antigenicity and antiviral susceptibility of the pandemic virus. Throughout the pandemic, CDC will provide updated instructions on the collection of clinical and epidemiologic data that should accompany isolates. CDC could ask some state public health laboratories to perform virus isolation or RT-PCR subtyping before sending specimens to CDC.
- CDC may work with the U.S.-based WHO collaborating laboratories, NREVSS laboratories, and/or Emerging Infectious Program sites (www.cdc.gov/ncidod/osr/site/eip/index.htm) to conduct special studies or establish additional laboratory-based surveillance systems to answer critical questions related to vaccine development or other aspects of the public health response. For example, CDC and state and local partners could conduct serosurveys to determine the number of persons who develop antibodies to the pandemic virus over time.

B. Laboratory support for clinicians

- When a pandemic begins, public health and clinical laboratories will scale up to manage increased numbers of requests for influenza testing. As part of this effort, CDC will work with state and local public health laboratories and the LRN to provide clinical laboratories with guidelines for safe handling, processing, and rapid diagnostic testing of clinical specimens from patients who meet the case definition for pandemic influenza.

If private laboratories perform RT-PCR testing during the early phase of an influenza pandemic, the results should be confirmed in consultation with the state public health laboratory.

- State and local health laboratories should provide local healthcare providers with:
  - Specimen submission forms that specify the clinical and epidemiologic data that should accompany clinical specimens sent to state public health laboratories. (During the early stages of a pandemic, clinicians should include information on patients' symptoms and risk factors, if known.)
  - Rapid communication of test results and reminders that a negative test result (especially by rapid diagnostic testing) might not rule out influenza and should not affect patient management or infection control decisions.
  - Guidance on the use of commercially available rapid diagnostic tests for the detection of influenza A. These tests may be used by physicians to supplement clinical diagnoses of pandemic influenza. Because the sensitivity of rapid diagnostic kits might not be optimal, physicians should take their positive and negative predictive values into consideration when interpreting test results (Appendix 6).
  - Guidance on which specimens to send to state public health laboratories as the pandemic continues.

C. Biocontainment procedures

During an influenza pandemic, laboratory procedures should be conducted under appropriate biosafety conditions:

- Commercial antigen detection testing for influenza should be conducted using BSL-2 work practices.
- Public health laboratories may conduct RT-PCR testing using BSL-2 work practices and virus isolation using BSL-3 practices with enhancements.

Additional information on laboratory biocontainment is provided in Appendix 4.

D. Occupational health issues for laboratory workers

To protect the health of laboratory workers during a pandemic, public health, clinical, and hospital laboratories should maintain the safety practices used during the Interpandemic and Pandemic Alert Periods. These include:

- Conducting laboratory procedures under appropriate biocontainment conditions
- Encouraging routine vaccination of all eligible laboratory personnel who are exposed to specimens from patients with respiratory infections

Guidelines for medical surveillance of laboratory personnel are provided in Appendix 7.

BOX 1. USE OF DIAGNOSTIC ASSAYS DURING AN INFLUENZA PANDEMIC

Public health and clinical laboratories will use different types of diagnostic tests for influenza at different stages of a pandemic. Each of the tests discussed below is described in detail in Appendix 1.

Virus Isolation

Virus isolation—growing the viral strain in cell culture—is the "gold standard" for influenza diagnostics because it confirms that the virus is infectious. During a pandemic, virus isolation followed by antigenic and genetic (sequencing) analysis will be used to characterize the earliest pandemic isolates, as well as to monitor their evolution during the pandemic. Laboratories that participate in the WHO Global Influenza Surveillance Network typically use virus isolation followed by hemagglutination inhibition (HAI), IFA staining, or RT-PCR to monitor circulating seasonal strains of influenza. If clinical and epidemiologic data suggest that a human case of influenza might be due to infection with avian influenza A (H5N1) or another highly pathogenic avian influenza strain (see Box 3), the virus should not be cultured except under BSL-3 conditions with enhancements. Laboratories that lack BSL-3 enhanced facilities may either perform RT-PCR subtyping using BSL-2 containment procedures or send the specimen to CDC for isolation and characterization.

Immunofluorescence Antibody Staining

IFA staining following virus isolation can be used to identify influenza types (A, B) and influenza A HA subtypes using a panel of specific antisera. In some cases, IFA can be used for direct testing of cells pelleted from original clinical samples. CDC's Influenza Branch produces and distributes a reagent kit to WHO collaborating laboratories that includes monoclonal antibodies for typing and subtyping currently circulating influenza viruses by IFA. Many laboratories use commercially available reagents to type influenza viruses by direct immunofluorescence tests (DFA).

RT-PCR Subtyping

Influenza specimens may also be typed and subtyped using RT-PCR, which does not require *in vitro* growth or isolation of virus. As of October 2005, CDC has trained scientists from 48 states to use RT-PCR subtyping to identify human and avian HA subtypes of public health concern. APHL members can access protocols and sequences of primers and probes that can be used for typing and subtyping on the APHL website.

Serologic Tests

Tests based on detection of antibodies in patient sera—e.g., enzyme-linked immunosorbent assay (ELISA), HAI, and microneutralization assay—can be used to retrospectively confirm influenza infection. Although microneutralization assay is the most comprehensive test for detection in humans of antibodies to avian influenza viruses, it is available in only a few state public health laboratories.

Rapid Diagnostic Tests

Several rapid diagnostic test kits based on antigen detection are commercially available for influenza. Laboratories in outpatient settings and hospitals can use these tests to detect influenza viruses within 30 minutes. Some tests can detect influenza A viruses (including avian strains); others can detect influenza A and B viruses without distinguishing between them, and some can distinguish between influenza A and B viruses. The type of specimens used in these tests (i.e., nasal wash/aspirate, nasopharyngeal swabs, or nasal swab or throat swab) may also vary. Like RT-PCR, rapid diagnostic tests do not require *in vitro* growth or isolation of virus. During a pandemic, rapid diagnostic tests will be widely used to distinguish influenza A from other respiratory illnesses. See Appendix 6 for additional information.

BOX 2. LABORATORY SUPPORT FOR SEASONAL INFLUENZA SURVEILLANCE

U.S. Collaborating Laboratories of the WHO Global Influenza Surveillance Network

All state and several large local public health laboratories, as well as about 25 tertiary-care hospital and academic center laboratories, participate as U.S. collaborating laboratories in the WHO Global Influenza Surveillance Network, which collects worldwide data on circulating strains of influenza viruses. These data are used to develop recommendations for the formulation of each year's influenza vaccines, as well as to detect new human influenza viruses that might have pandemic potential. CDC's Influenza Laboratory serves as the WHO Collaborating Center for Surveillance, Epidemiology, and Control of Influenza, along with the WHO Collaborating Centers for Reference and Research on Influenza in Australia, Japan, and the United Kingdom.

The U.S.-based WHO collaborating laboratories provide CDC with weekly reports of laboratory-confirmed cases of influenza A and B viruses, by age group. These laboratories typically use virus isolation followed by antigenic testing with IFA staining or HAI—or by molecular testing with RT-PCR—to identify known subtypes of human influenza viruses. If unusual subtypes are detected, or if the specimens cannot be subtyped using available techniques, the specimens are sent to CDC for further testing.

NREVSS Collaborating Laboratories

The National Respiratory and Enteric Virus Surveillance System (NREVSS; http://www.cdc.gov/ncidod/dvrd/revb/nrevss/) includes more than 90 laboratories throughout the country, including many hospital laboratories, some state public health laboratories, and a few private commercial laboratories. About 40 of the NERVSS laboratories are also WHO collaborating laboratories.

Like the WHO collaborating laboratories, NREVSS laboratories provide CDC with weekly reports of laboratory-confirmed cases of influenza A and B viruses. These laboratories typically test respiratory specimens with commercially available rapid diagnostic tests. Several NREVSS laboratories also perform virus isolation followed by rapid diagnostic tests or antigenic typing by IFA. If untypable viruses or unusual subtypes are detected, the specimens are sent to the state public health laboratory or to CDC for further testing.

BOX 3. AVIAN INFLUENZA STRAINS WITH HIGH AND LOW PATHOGENICITY

The U.S. Department of Agriculture (USDA) classifies avian influenza viruses as low pathogenic avian influenza (LPAI) viruses or highly pathogenic avian influenza (HPAI) viruses, based on characteristics of a virus' hemagglutinin cleavage site or its virulence in birds, as determined by laboratory testing. LPAI strains are endemic in wild birds worldwide and are responsible for most avian influenza outbreaks in poultry. LPAI strains with H5 and H7 subtypes sometimes evolve into highly pathogenic forms. HPAI strains are extremely contagious and cause severe illness and high mortality rates in poultry.

LPAI strains include:

- H5N2, the cause of poultry outbreaks in New York, Maine, and California in 2002
- H7N2, the cause of poultry outbreaks in Delaware, Maryland, and New Jersey in 2004

HPAI strains include:

- H5N1, the cause of major poultry outbreaks in Southeast Asia
- H7N7, the cause of a 2003 outbreak in the Netherlands
- H7N3, the cause of a 2004 outbreak in British Columbia
- H5N2, the cause of a 2004 outbreak in poultry in Texas

The 2004 outbreak in Texas was the first HPAI outbreak in the United States since a previous outbreak of H5N2 in 1983-84 in the northeastern United States. The 1983-84 disease control effort involved the destruction of approximately 17 million birds and cost more than $70 million.

Although avian influenza A viruses do not usually infect humans, several instances of human infections of avian influenza have been reported since 1997. Cases of avian influenza infection in humans are apparently caused by contact with infected poultry or with surfaces contaminated with avian influenza viruses.

LPAI strains associated with human infection include:

- H9N2, which caused three cases of influenza-like illness in Hong Kong between 1999 and 2003, and other cases in China in 1998 and 1999
- H7N2, which was detected by serology in one person involved in the culling of sick chickens during the response to a poultry outbreak in Virginia in 2002, and was isolated from a New York resident in 2003 (unknown source of the infection)

HPAI viruses associated with human infection include:

- H5N1, which caused 51 deaths in Southeast Asia between January 2004 and April 2005
- H7N7, which caused the death of a veterinarian as well as 83 cases of mild human disease (including conjunctivitis) during the 2003 poultry outbreak in the Netherlands.
- H7N3, which caused 2 cases of very mild human disease (conjunctivitis, headache) in persons culling sick poultry in British Columbia in 2004

APPENDIX 1. INFLUENZA DIAGNOSTIC ASSAYS

Among the several types of assays used to detect influenza, rapid antigen tests, reverse-transcription polymerase chain reaction (RT-PCR), viral isolation, immunofluorescence assays (IFA), and serology are the most commonly used. The sensitivity and specificity of any test for influenza will vary by the laboratory that performs the test, the type of test used, and the type of specimen tested. A chart that lists influenza diagnostic procedures and commercially available rapid diagnostic tests follows more detailed descriptions provided below.

Virus Isolation

Biocontainment level: Interpandemic and Pandemic Alert Periods – BSL-3 with enhancements; Pandemic Period – BSL-2

Virus isolation is a highly sensitive and very useful technique when the clinical specimens are of good quality and have been collected in a timely manner (optimally within 3 days of the start of illness). Isolation of a virus in cell culture along with the subsequent identification of the virus by immunologic or genetic techniques are standard methods for virus diagnosis. Virus isolation amplifies the amount of virus from the original specimen, making a sufficient quantity of virus available for further antigenic and genetic characterization and for drug-susceptibility testing if required. Virus isolation is considered the "gold standard" for diagnosis of influenza virus infections.

> Highly pathogenic avian influenza (HPAI) viruses are BSL-3 agents. During the Interpandemic and Pandemic Alert Periods, laboratories should attempt to culture HPAI viruses—as well as other influenza viruses with pandemic potential—only under BSL-3 conditions with enhancements in order to optimally reduce the risk of a novel influenza virus subtype spreading to persons or animals. During the Pandemic Period, biocontainment of BSL-2 is appropriate to prevent laboratory-acquired infection and the virus will already be widespread.

In recent years, the use of cell lines has surpassed the use of embryonated eggs for culturing of influenza viruses, although only viruses grown in embryonated eggs are used as seed viruses for vaccine production. Because standard isolation procedures require several days to yield results, they should be used in combination with the spin-amplification shell-vial method. The results of these assays can be obtained in 24–72 hours, compared to an average of 4.5 days using standard culture techniques. Spin-amplification should not be performed using 24-well plates because of increased risk of cross-contamination. The most effective combination of cell lines recommended for public health laboratories is primary rhesus monkey for standard culture, along with Madin Darby Canine Kidney (MDCK) in shell vial.[1] The use of these two cell lines in combination has demonstrated maximum sensitivity over time for recovery of evolving influenza strains. Some clinical laboratories have recently reported good isolation rates using commercially available cell-line mixed-cell combinations; however, data are lacking on the performance of these mixed cells with new subtypes of Influenza A viruses.

Appropriate clinical specimens for virus isolation include nasal washes, nasopharyngeal aspirates, nasopharyngeal and throat swabs, tracheal aspirates, and bronchoalveolar lavage. Ideally, specimens should be collected within 72 hours of the onset of illness.

Viral culture isolates are used to provide specific information regarding circulating influenza subtypes and strains. This information is needed to compare current circulating influenza strains with vaccine strains, to guide decisions on influenza treatment and chemoprophylaxis, and to select vaccine strains for the coming year. Virus isolates also are needed to monitor

[1] The shell-vial technique is described in: *Manual of Clinical Virology,* 3rd edition. Steven Specter, Richard Hodinka, and Stephen Young, eds. ASM Press, 2000.

the emergence of antiviral resistance and of novel influenza A subtypes that might pose a pandemic threat. During outbreaks of influenza-like illness, viral culture may help identify other causes of illness when influenza is not the etiology (except when using MDCK cells or the MDCK shell-vial technique).

Immunofluorescence Assays

Biocontainment level: BSL-2 when performed directly on clinical specimens; if used on cultures for earlier detection of virus, biocontainment recommendations for viral culture apply

Direct (DFA) or indirect (IFA) immunofluorescence antibody staining of virus-infected cells is a rapid and sensitive method for diagnosis of influenza and other viral infections. DFA and IFA can also be used to type and subtype influenza viruses using commercially available monoclonal antibodies specific for the influenza virus HA. The sensitivity of these methods is greatly influenced by the quality of the isolate, the specificity of the reagents used, and the experience of the person(s) performing, reading, and interpreting the test.

Although IFA can be used to stain smears of clinical specimens directly, when rapid diagnosis is needed it is preferable to first increase the amount of virus through growth in cell culture. For HPAI isolates, attempts to culture the virus should be made only under BSL-3 conditions with enhancements.

Reverse-Transcription Polymerase Chain Reaction (RT-PCR)

Biocontainment level: BSL-2

PCR can be used for rapid detection and subtyping of influenza viruses in respiratory specimens. Because the influenza genome consists of single-stranded RNA, a complementary DNA (cDNA) copy of the viral RNA must be synthesized using the reverse-transcriptase (RT) enzyme prior to the PCR reaction.

Laboratories can obtain CDC protocols and sequences of primers and probes for rapid RT-PCR detection of human and avian HA subtypes of current concern at the APHL website (available for members only). These protocols use real-time RT-PCR methods with fluorescent-labeled primers that allow automatic, semi-quantitative estimation of the input template. The RT-PCR results are analyzed and archived electronically, without the need for gel electrophoresis and photographic recording. A large number of samples may be analyzed at the same time, reducing the risk of carry-over contamination.

As with all PCR assays, interpretation of real-time RT-PCR tests must account for the possibility of false-negative and false-positive results. False-negative results can arise from poor sample collection or degradation of the viral RNA during shipping or storage. Application of appropriate assay controls that identify poor-quality samples (e.g., an extraction control and, if possible, an inhibition control) can help avoid most false-negative results. [2]

The most common cause of false-positive results is contamination with previously amplified DNA. The use of real-time RT-PCR helps mitigate this problem by operating as a contained system. A more difficult problem is the cross-contamination that can occur between specimens during collection, shipping, and aliquoting in the laboratory. Use of multiple negative control samples in each assay and a well-designed plan for confirmatory testing can help ensure that laboratory contamination is detected and that negative specimens are not inappropriately identified as influenza-positive.

Specimens that test positive for a novel subtype of influenza virus should be forwarded to CDC for confirmatory testing. (Due to the possibility of contamination, it is important to provide original clinical material.) All laboratory results should be interpreted in the context of the clinical and epidemiologic information available on the patient.

[2] CDC is working with the private sector to provide inactivated RNA virus for use as RT-PCR controls for influenza A (H5) testing in LRN laboratories. CDC is working with USDA to resolve any permit issues that might affect the ability of LRN members to use these controls.

Rapid Diagnostic Tests

Biocontainment level: BSL-2

Commercial rapid diagnostic tests can be used in outpatient settings to detect influenza viruses within 30 minutes. These rapid tests differ in the types of influenza viruses they can detect and in their ability to distinguish among influenza types. Different tests can 1) detect influenza A viruses only (including avian strains); 2) detect both influenza A and B viruses, without distinguishing between them; or 3) detect both influenza A and B viruses and distinguish between them.

The types of specimens acceptable for use (i.e., nasal wash/aspirate, nasopharyngeal swab, or nasal swab and throat swab) also vary by test. The specificity and, in particular, the sensitivity of rapid tests are lower than for viral culture and vary by test and specimen tested. The majority of rapid tests are >70% sensitive and >90% specific. Thus, as many as 30% of samples that would be positive for influenza by viral culture may give a negative rapid test result with these assays.

When interpreting results of a rapid influenza test, physicians should consider the level of influenza activity in the community. When influenza prevalence is low, positive rapid test results should be independently confirmed by culture or RT-PCR. When influenza is known to be circulating, clinicians should consider confirming negative tests with viral culture or other means because of the lower sensitivity of the rapid tests. Package inserts and the laboratory performing the test should be consulted for more details regarding use of rapid diagnostic tests. Additional information on diagnostic testing is provided at: http://www.cdc.gov/flu/professionals/labdiagnosis.htm. Detailed information on the use of rapid diagnostics tests is provided in Appendix 6.

Serologic Tests[3]

Hemagglutination Inhibition (HAI)

Biocontainment level: BSL-2

Serologic testing can be used to identify recent infections with influenza viruses. It can be used when the direct identification of influenza viruses is not feasible or possible (e.g., because clinical specimens for virus isolation cannot be obtained, cases are identified after shedding of virus has stopped, or the laboratory does not have the resources or staff to perform virus isolation).

Since most human sera contain antibodies to influenza viruses, serologic diagnosis requires demonstration of a four-fold or greater rise in antibody titer using paired acute and convalescent serum samples. HAI is the preferred diagnostic test for determining antibody rises. In general, acute-phase sera should be collected within one week of illness onset, and convalescent sera should be collected 2–3 weeks later.

There are two exceptions in which the collection of single serum samples can be helpful in the diagnosis of influenza. In investigations of outbreaks due to novel viruses, testing of single serum samples has been used to identify antibody to the novel virus. In other outbreak investigations, antibody test results from single specimens collected from persons in the convalescent phase of illness have been compared with results either from age-matched persons in the acute phase of illness or from non-ill controls. In such situations, the geometric mean titers between the two groups to a single influenza virus type or subtype can be compared. In general, these approaches are not optimal, and paired sera should be collected whenever possible.

Because HAI titers of antibodies in humans infected with avian influenza viruses are usually very low or even undetectable, more sensitive serologic tests, such as microneutralization, may be needed.

[3] Enzyme-linked immunoassay (EIA) is not included on this list because of non-specificity issues. Complement fixation is not included because it is currently out of use.

Microneutralization Assay

Biocontainment level: Interpandemic and Pandemic Alert Periods – BSL-3 with enhancements; Pandemic Period – BSL-2

The virus neutralization test is a highly sensitive and specific assay for detecting virus-specific antibody in animals and humans. The neutralization test is performed in two steps: 1) a virus-antibody reaction step, in which the virus is mixed with antibody reagents, and 2) an inoculation step, in which the mixture is inoculated into a host system (e.g. cell cultures, embryonated eggs, or animals). The absence of infectivity constitutes a positive neutralization reaction and indicates the presence of virus-specific antibodies in human or animal sera.

The virus neutralization test gives the most precise answer to the question of whether or not a person has antibodies that can neutralize the infectivity of a given virus strain. The neutralization test has several additional advantages for detecting antibody to influenza virus. First, the assay primarily detects antibodies to the influenza virus HA and thus can identify functional, strain-specific antibodies in animal and human serum. Second, since infectious virus is used, the assay can be developed quickly upon recognition of a novel virus and before suitable purified viral proteins become available for use in other assays.

The microneutralization test is a sensitive and specific assay for detecting virus-specific antibody to avian influenza A (H5N1) in human serum and potentially for detecting antibody to other avian subtypes. Microneutralization can detect H5-specific antibody in human serum at titers that cannot be detected by HAI. Because antibody to avian influenza subtypes is presumably low or absent in most human populations, single serum samples can be used to screen for the prevalence of antibody to avian viruses. However, if infection of humans with avian viruses is suspected, the testing of paired acute and convalescent sera in the microneutralization test would provide a more definitive answer regarding the occurrence of infection. Conventional neutralization tests for influenza viruses based on the inhibition of cytopathogenic effect (CPE)-formation in MDCK cell cultures are laborious and rather slow, but in combination with rapid culture assay principles the neutralization test can yield results within 2 days. For HPAI viruses, neutralization tests should be performed at BSL-3 enhanced conditions.

QUICK REFERENCE CHART OF INFLUENZA DIAGNOSTIC TESTS[1]

(From: *Prevention and Control of Influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP).* MMWR 2004;53(RR-6):1-40.

Procedure	Influenza Types Detected	Acceptable Specimens	Time for Results	Rapid result available
Viral culture	A and B	nasal wash/aspirate, NP swab,2 nasal aspirate, nasal swab and throat swab, sputum	5–10 days[3]	No
Immunofluorescence Antibody Staining	A and B	nasal wash/aspirate, NP swab,2 nasal aspirate, nasal swab and throat swab, sputum	2–4 hours	No
RT-PCR[5]	A and B	nasal wash/aspirate, NP swab,2 nasal aspirate, throat swab, bronchial wash, nasal aspirate, sputum	Hours	No
Serology	A and B	paired acute/convalescent serum samples6	>2 weeks	No
Rapid Diagnostic Tests				
Directigen Flu A[7] (Becton-Dickinson)	A	NP swab,2 throat swab, nasal wash, nasal aspirate	See insert	Yes
Directigen Flu A+B[7, 9] (Becton-Dickinson)	A and B	NP swab,2 throat swab, nasal wash, nasal aspirate	See insert	Yes
FLU OIA[7] (Thermo Electron)	A and B[4]	NP swab,2 throat swab, nasal aspirate, sputum	See insert	Yes
FLU OIA A/B[7, 9] (Thermo Electron)	A and B	NP swab,2 throat swab, nasal aspirate, sputum	See insert	Yes
XPECT Flu A/B[7, 9] (Remel)	A and B	Nasal wash, NP swab,2 throat swab	See insert	Yes
NOW Flu A Test[7, 9] NOW Flu B Test[7, 9] (Binax)	A B	Nasal wash, NP swab2 Nasal wash, NP swab2	See insert	Yes Yes
QuickVue Influenza Test[8] (Quidel)	A and B[4]	NP swab,2 nasal wash, nasal aspirate	See insert	Yes
QuickVue Influenza A+B Test[8] (Quidel)	A and B[9] A	NP swab,2 nasal wash, nasal aspirate	See insert	Yes
SAS Influenza A[7, 9] SAS Influenza B[7, 9]	B	NP wash,2 NP aspirate2 NP wash,2 NP aspirate2	See insert	Yes Yes
ZstatFlu[8] (ZymeTx)	A and B[4]	throat swab	See insert	Yes

[1] The list might not include all FDA-approved test kits.
[2] NP = nasopharyngeal
[3] Shell-vial culture, if available, may reduce time for results to 2 days.
[4] Does not distinguish between influenza A and B virus infections.
[5] RT-PCR = reverse-transcription polymerase chain reaction
[6] A fourfold or greater rise in antibody titer from the acute- (collected within the first week of illness) to the convalescent-phase sample (collected 2–4 weeks after the acute sample) indicates recent infection.
[7] Moderately complex test that requires specific laboratory certification
[8] CLIA-waived test. Can be used in any office setting. Requires a certificate of waiver or higher laboratory certification
[9] Distinguishes between influenza A and B virus infections.

Disclaimer: Use of trade names or commercial sources is for identification only and does not imply endorsement by the Centers for Disease Control and Prevention or the Department of Health and Human Services.

APPENDIX 2. INTERIM RECOMMENDATIONS: ENHANCED U.S. SURVEILLANCE AND DIAGNOSTIC EVALUATION TO IDENTIFY CASES OF HUMAN INFECTION WITH AVIAN INFLUENZA A (H5N1)

NOTE: This guidance pertains to the avian influenza A (H5N1) situation in October 2005. CDC will provide updated guidance for avian influenza A (H5N1) and for new situations, as needed, through the Health Alert Network (HAN).

Enhanced surveillance efforts by state and local health departments, hospitals, and clinicians are needed to identify patients at increased risk for influenza A (H5N1). Interim recommendations include the following:

Testing for avian influenza A (H5N1) is indicated for **hospitalized** patients with:

- Radiographically confirmed pneumonia, acute respiratory distress syndrome (ARDS), or other severe respiratory illness for which an alternative diagnosis has not been established, *and*
- History of travel within 10 days of symptom onset to a country with documented avian influenza A (H5N1) infections in poultry and/or humans. (For a regularly updated listing of H5N1-affected countries, see the OIE website at http://www.oie.int/eng/en_index.htm and the WHO website at http://www.who.int/en/).

or

Testing for avian influenza A (H5N1) should be considered on a case-by-case basis in consultation with state and local health departments for **hospitalized or ambulatory** patients with:

- Documented temperature of >100.4°F (>38°C), *and*
- One or more of the following: cough, sore throat, or shortness of breath, *and*
- History of close contact either with poultry (e.g., visited a poultry farm, a household raising poultry, or a bird market) in an H5N1-affected country, or with a known or suspected human case of influenza A (H5N1) within 10 days prior to onset of symptoms.

APPENDIX 3. REFERENCE TESTING GUIDELINES FOR POTENTIAL PANDEMIC STRAINS OF INFLUENZA

State and local laboratories may conduct initial testing on patient specimens for influenza A or potential highly pathogenic strains, if laboratory capacity is available. Due to the spread of avian influenza A (H5N1) in poultry in Asia, laboratories should be on the alert for avian and human H5 viruses. Procedures for diagnosis of human cases of influenza A (H5N1) are provided in Appendix 2. Influenza A viruses other than currently circulating H1 and H3 subtypes should also be considered as potentially pandemic if detected in humans.

- State/local laboratories should send specimens to CDC if:
  - A sample tested by the state or local laboratory is positive for H5 or another novel subtype;

    Note: *A laboratory should test for influenza A (H5) only if it is able to do so by PCR or has a BSL-3-enhanced facility for influenza A(H5) viral culture.*

  or

  - A sample from a patient who meets the clinical and epidemiologic criteria for possible infection with a potentially pandemic virus is positive for influenza A by RT-PCR or rapid antigen detection,* is negative for influenza A(H1) and A(H3), and the referring jurisdiction is not equipped to test for specific strains;

  or

  - The referring jurisdiction is not equipped to test samples for novel influenza viruses by RT-PCR and is requesting testing at CDC.

Shipping procedures for potential pandemic strains of influenza are provided in Appendix 5.

**Because the sensitivity of commercially available rapid diagnostic tests for influenza may not always be optimal, CDC will also accept specimens taken from persons who meet the clinical and epidemiological criteria even if they test negative by influenza rapid diagnostic testing—if PCR assays are not available at the state laboratory.*

APPENDIX 4. LABORATORY BIOSAFETY GUIDELINES FOR HANDLING AND PROCESSING SPECIMENS OR ISOLATES OF NOVEL INFLUENZA STRAINS

Key Messages

- Commercial antigen detection testing for influenza may be conducted under BSL-2 containment conditions if a Class II biological safety cabinet is used.
- Clinical specimens from suspected novel influenza cases may be tested by RT-PCR using standard BSL-2 work practices in a Class II biological safety cabinet for initial processing of patient specimens.
- If a specimen is confirmed positive for influenza A (H5N1) by RT-PCR, additional testing should be performed only under BSL-3 conditions with enhancements. CDC's Influenza Branch should be informed immediately by contacting the CDC Director's Emergency Operations Center (DEOC) at 770-488-7100.
- A detailed description of recommended facilities, practices, and protective equipment for the various laboratory biosafety levels can be found in the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL) manual at www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4toc.htm
- BSL-3 with enhancements and Animal Biosafety Level 3 include: all BSL-3 practices, procedures, and facilities, plus the use of negative-pressure, HEPA-filtered respirators or positive air-purifying respirators, and clothing change and personal showering protocols. Additional practices and/or restrictions may be added as conditions of USDA-APHIS permits. Registration of personnel and facilities with the Select Agent Program is required for work with highly pathogenic avian influenza (HPAI) viruses, which are classified as agricultural select agents.

- State and local public health laboratories may test clinical specimens from suspected novel influenza cases by RT-PCR using standard BSL-2 work practices in a Class II biological safety cabinet. Commercial rapid antigen detection testing may also be conducted under BSL-2 biocontainment conditions.
- Highly pathogenic avian influenza A (H5) and A (H7) viruses are classified as select agents. USDA regulations require that these viruses (as well as exotic low pathogenic avian influenza viruses) be handled under BSL-3 laboratory containment conditions, with enhancements (i.e., controlled-access double-door entry with change room and shower, use of respirators, decontamination of all wastes, and showering of all personnel). Laboratories that work with these viruses must be certified by USDA.
- Laboratories should not perform virus isolation on respiratory specimens from patients who may be infected with an avian influenza virus unless stringent BSL-3 enhanced containment conditions can be met and diagnostic work can be kept separate from studies with other human influenza A viruses (i.e., H1 or H3). Therefore, respiratory virus cultures should not be performed in most clinical laboratories. Cultures for patients suspected of having influenza A (H5N1) infection should be sent only to state laboratories with appropriate BSL-3 with enhancement containment facilities or to CDC.

APPENDIX 5. GUIDELINES FOR COLLECTING AND SHIPPING SPECIMENS FOR INFLUENZA DIAGNOSTICS

Key Messages

- Appropriate specimens for influenza testing vary by type of test.
- Before collecting specimens, review the infection control precautions are described in Supplement 3.

I. RESPIRATORY SPECIMENS[4]

Eight types of respiratory specimens may be collected for viral and/or bacterial diagnostics:

1) nasopharyngeal wash/aspirates, 2) nasopharyngeal swabs, 3) oropharyngeal swabs, 4) broncheoalveolar lavage, 5) tracheal aspirate, 6) pleural fluid tap, 7) sputum, and 8) autopsy specimens. Nasopharyngeal wash/aspirates are the specimen of choice for detection of most respiratory viruses and are the preferred specimen type for children aged <2 years.

Respiratory specimens for detection of most respiratory pathogens, and influenza in particular, are optimally collected within the first 3 days of the onset of illness. Before collecting specimens, review the infection control precautions in **Supplement 4**.

A. Collecting specimens from the upper respiratory tract

1. Nasopharyngeal wash/aspirate

- Have the patient sit with head tilted slightly backward.
- Instill 1 ml–1.5 ml of nonbacteriostatic saline (pH 7.0) into one nostril. Flush a plastic catheter or tubing with 2 ml–3 ml of saline. Insert the tubing into the nostril parallel to the palate. Aspirate nasopharyngeal secretions. Repeat this procedure for the other nostril.
- Collect the specimens in sterile vials. Label each specimen container with the patient's ID number and the date collected.
- If shipping domestically, use cold packs to keep the sample at 4°C. If shipping internationally, pack in dry ice (see shipping instructions below).

2. Nasopharyngeal or oropharyngeal swabs

- Use only sterile dacron or rayon swabs with plastic shafts. Do **not** use calcium alginate swabs or swabs with wooden sticks, as they may contain substances that inactivate some viruses and inhibit PCR testing.
- To obtain a **nasopharyngeal swab**, insert a swab into the nostril parallel to the palate. Leave the swab in place for a few seconds to absorb secretions. Swab both nostrils.
- To obtain an **oropharyngeal swab**, swab the posterior pharynx and tonsillar areas, avoiding the tongue.
- Place the swabs immediately into sterile vials containing 2 ml of viral transport media. Break the applicator sticks off near the tip to permit tightening of the cap. Label each specimen container with the patient's ID number and the date the sample was collected.
- If shipping domestically, use cold packs to keep the sample at 4°C. If shipping internationally, pack in dry ice (see shipping instructions below).

[4] All types of respiratory specimens may used in RT-PCR tests. Fresh-frozen unfixed tissue specimens may also be submitted for RT-PCR.

B. Collecting specimens from the lower respiratory tract

1. Broncheoalveolar lavage, tracheal aspirate, or pleural fluid tap

- During bronchoalveolar lavage or tracheal aspirate, use a double-tube system to maximum shielding from oropharyngeal secretions.
- Centrifuge half of the specimen, and fix the cell pellet in formalin. Place the remaining unspun fluid in sterile vials with external caps and internal O-ring seals. If there is no internal O-ring seal, then seal tightly with the available cap and secure with Parafilm®. Label each specimen container with the patient's ID number and the date the sample was collected.
- If shipping domestically, use cold packs to keep the sample at 4°C. If shipping internationally, ship fixed cells at room temperature and unfixed cells frozen (see shipping instructions below).

2. Sputum

- Educate the patient about the difference between sputum and oral secretions.
- Have the patient rinse the mouth with water and then expectorate deep cough sputum directly into a sterile screw-cap sputum collection cup or sterile dry container.
- If shipping domestically, use cold packs to keep the sample at 4°C. If shipping internationally, pack in dry ice (see shipping instructions below).

II. BLOOD COMPONENTS

Both acute and convalescent serum specimens should be collected for antibody testing. Collect convalescent serum specimens 2–4 weeks after the onset of illness. To collect serum for antibody testing:

- Collect 5 ml–10 ml of whole blood in a serum separator tube. Allow the blood to clot, centrifuge briefly, and collect all resulting sera in vials with external caps and internal O-ring seals. If there is no internal O-ring seal, then seal tightly with the available cap and secure with Parafilm®.
- The minimum amount of serum preferred for each test is 200 microliters, which can easily be obtained from 5 ml of whole blood. A minimum of 1 cc of whole blood is needed for testing of pediatric patients. If possible, collect 1 cc in an EDTA tube and in a clotting tube. If only 1cc can be obtained, use a clotting tube.
- Label each specimen container with the patient's ID number and the date the specimen was collected.
- If unfrozen and transported domestically, ship with cold packs to keep the sample at 4°C. If frozen or transported internationally, ship on dry ice.

III. AUTOPSY SPECIMENS

CDC can perform immunohistochemical (IHC) staining for influenza A (H5) viruses on autopsy specimens. Viral antigens may be focal and sparsely distributed in patients with influenza, and are most frequently detected in respiratory epithelium of large airways. Larger airways (particularly primary and segmental bronchi) have the highest yield for detection of influenza viruses by IHC staining. Collection of the appropriate tissues ensures the best chance of detecting the virus by (IHC) stains.

- If influenza is suspected, a minimum total of 8 blocks or fixed-tissue specimens representing samples from each of the following sites should be obtained and submitted for evaluation:
  - Central (hilar) lung with segmental bronchi
  - Right and left primary bronchi
  - Trachea (proximal and distal)
  - Representative pulmonary parenchyma from right and left lung

In addition, representative tissues from major organs should be submitted for evaluation. In particular, for patients with suspected myocarditis or encephalitis, specimens should include myocardium (right and left ventricle) and CNS (cerebral cortex, basal ganglia, pons, medulla, and cerebellum). Specimens should be included from any other organ showing significant gross or microscopic pathology.

- Specimens may be submitted as:
  - Fixed, unprocessed tissue in 10% neutral buffered formalin, or
  - Tissue blocks containing formalin-fixed, paraffin-embedded specimens, or
  - Unstained sections cut at 3 microns placed on charged glass slides (10 slides per specimen)
- Specimens should be sent at room temperature (**NOT FROZEN**).
- Fresh-frozen unfixed tissue specimens may be submitted for RT-PCR.
- Include a copy of the autopsy report (preliminary, or final if available), and a cover letter outlining a brief clinical history and the submitter's full name, title, complete mailing address, phone, and fax numbers, in the event that CDC pathologists require further information. Referring pathologists may direct specific questions to CDC pathologists. The contact number for the Infectious Disease Pathology Activity is 404-639-3133, or the pathologists can be contacted 24 hours a day, 7 days a week through the CDC Emergency Response Hotline at 770-488-7100.

IV. SHIPPING INSTRUCTIONS

- State and local health departments should call the CDC Emergency Response Hotline (770-488-7100) before sending specimens for influenza A reference testing. This number is available 24 hours a day, 7 days a week. Hotline staff will notify a member of the Influenza Branch who will contact the health department to answer questions and provide guidance. In some cases, the state health department may arrange for a clinical laboratory to send samples directly to CDC.
- Specimens should be sent by Priority Overnight Shipping for receipt within 24 hours. Samples (such as fresh-frozen autopsy samples for RT-PCR or other clinical materials) may be frozen at –70 if the package cannot be shipped within a specified time (e.g., if the specimen is collected on a Friday but cannot be shipped until Monday).
- When sending clinical specimens, include the specimen inventory sheet (see below), include the assigned CDC case ID number, and note "Influenza surveillance" on all materials and specimens sent.

Include the CDC case ID number on all materials forwarded to CDC. Protocols for standard interstate shipment of etiologic agents should be followed, and are available at http://www.cdc.gov/od/ohs/biosfty/shipregs.htm. All shipments must comply with current DOT/IATA shipping regulations.

V. INFLUENZA SPECIMEN INVENTORY SHEET

CDC CASE ID:

List specimens sent to the CDC

Select a SOURCE* from the following list for each specimen: Serum (acute), serum (convalescent), NP swab, NP aspirate/wash, broncheoalveolar lavage specimen (BAL), OP swab, tracheal aspirate, or tissue.

Specimen Type #1:

❑ Clinical Material
❑ Extracted RNA
❑ Virus Isolate

Source*:_____

Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Specimen Type #2:

❑ Clinical Material
❑ Extracted RNA
❑ Virus Isolate

Source*:_____

Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Specimen Type #3:

❑ Clinical Material
❑ Extracted RNA
❑ Virus Isolate

Source*:_____

Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Specimen Type #4:

❑ Clinical Material
❑ Extracted RNA
❑ Virus Isolate

Source*:_____

Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Specimen Type #5:

❑ Clinical Material
❑ Extracted RNA
❑ Virus Isolate

Source*:_____

Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Carrier: _____ Tracking _____

APPENDIX 6. RAPID DIAGNOSTIC TESTING FOR INFLUENZA

The following information in this appendix is designed to assist clinicians and clinical laboratory directors in the use of rapid diagnostic tests during interpandemic influenza seasons. During an influenza pandemic, one or more of these tests may be sensitive and specific enough to be used by clinicians to supplement clinical diagnoses of pandemic influenza. However, clinicians should be reminded that a negative test result might not rule out pandemic influenza and should not affect patient management or infection control decisions.

I. INFORMATION FOR CLINICIANS

A. Background

Rapid diagnostic tests for influenza can help in the diagnosis and management of patients who present with signs and symptoms compatible with influenza. They also are useful for helping to determine whether institutional outbreaks of respiratory disease might be due to influenza. In general, rapid diagnostic testing for influenza should be done when the results will affect a clinical decision.

Rapid diagnostic testing can provide results within 30 minutes.

B. Reliability and interpretation of rapid test results

The reliability of rapid diagnostic tests depends largely on the conditions under which they are used. Understanding some basic considerations can minimize being misled by false-positive or false-negative results.

Median sensitivities of rapid diagnostic tests are generally ~70%–75% when compared with viral culture, but median specificities of rapid diagnostic tests for influenza are approximately 90%–95%. False-positive (and true negative) results are more likely to occur when disease prevalence in the community is low, which is generally at the beginning and end of the influenza season. False-negative (and true positive) results are more likely to occur when disease prevalence is high in the community, which is typically at the height of the influenza season.

C. Minimizing the occurrence of false results

- Use rapid diagnostic tests that have high sensitivity and specificity.
- Collect specimens as early in the illness as possible (within 4–5 days of symptom onset).
- Follow the manufacturer's instructions, including those for handling of specimens.
- Consider sending specimens for viral culture when:
  - Community prevalence of influenza is low and the rapid diagnostic test result is positive, *or*
  - Disease prevalence is high but the rapid diagnostic test result is negative.

  (Contact your local or state health department for information about influenza activity.)

D. For further information

- Information about influenza is available at the CDC influenza website (www.cdc.gov/flu) or from the CDC Flu Information Line (800-CDC-INFO [English and Spanish]; 800-243-7889 [TTY]).
- For more information about influenza diagnostics, contact your state laboratory or state health department (http://www.cdc.gov/other.htm#states).
- Additional resources:
  - Association of Public Health Laboratories: http://www.aphl.org/Public_Health_Labs/index.cfm

- Weekly U.S. influenza activity reports: http://www.cdc.gov/flu/weekly/fluactivity.htm
- CDC Clinician Outreach and Communication Activity: http://www.bt.cdc.gov/coca/index.asp
- CDC website: http://www.cdc.gov/flu/professionals/labdiagnosis.htm

II. INFORMATION FOR CLINICAL LABORATORY DIRECTORS

A. Background

Rapid diagnostic tests for influenza are screening tests for influenza virus infection; they can provide results within 30 minutes. The use of commercial influenza rapid diagnostic tests by laboratories and clinics has increased substantially in recent years. At least ten rapid influenza tests have been approved by the U.S. Food and Drug Administration (FDA) (see Appendix 1).

Rapid tests differ in some important respects. Some can identify influenza A and B viruses and distinguish between them; some can identify influenza A and B viruses but cannot distinguish between them. Some tests are waived from requirements under the Clinical Laboratory Improvement Amendments of 1988 (CLIA). Most tests can be used with a variety of specimen types, but sensitivity and specificity can vary with specimen type. FDA approval is based upon specific specimen types.

Rapid tests vary in terms of sensitivity and specificity when compared with viral culture. Product insert information and research publications indicate that median sensitivities are approximately 70%–75% and median specificities are approximately 90%–95%.

Specimens to be used with rapid tests generally should be collected as close as possible to the start of symptoms and usually no more than 4–5 days later in adults. In very young children, influenza viruses can be shed for longer periods; therefore, in some instances, testing for a few days after this period may still be useful. Test sensitivity will be greatest in children, who generally have higher viral titers, if the specimen is obtained during the first 2 days of illness, and if the clinician or laboratory has more experience performing the test. The quality of the specimen tested also is critical for test sensitivity.

B. Accuracy depends on disease prevalence

The positive and negative predictive values of rapid tests vary considerably depending on the prevalence of influenza in the community. False-positive (and true negative) influenza test results are more likely to occur when disease prevalence is low, which is generally at the beginning and end of the influenza season. False-negative (and true positive) influenza test results are more likely to occur when disease prevalence is high, which is typically at the height of the influenza season.

1. Clinical considerations when influenza prevalence is low

When disease prevalence is low, the positive-predictive value (PPV) is low and false-positive test results are more likely. By contrast, the negative-predictive value (NPV) is high when disease prevalence is low, and negative results are more likely to be truly negative (see Graphs 1 and 2).

If flu prevalence is...	**and specificity is...**	**then PPV is...**	**false-positive rate is...**
VERY LOW (2.5%)	POOR (80%)	V POOR (6%–12%)	V. HIGH (88%–94%)
VERY LOW (2.5%)	GOOD (98%)	POOR (39%–56%)	HIGH (44%–61%)
MODERATE (20%)	POOR (80%)	POOR (38%–56%)	HIGH (44%–62%)
MODERATE (20%)	GOOD (98%)	GOOD (86%–93%)	LOW (7%–14%)

Interpretation of positive results should take into account the clinical characteristics of the case-patient. If an important clinical decision is affected by the test result, the rapid test result should be confirmed by another test, such as viral culture or PCR.

2. Clinical considerations when influenza prevalence is high

When disease prevalence is relatively high, the NPV is low and false-negative test results are more likely. By contrast, when disease prevalence is high, the PPV is high and positive results are more likely to be true (see Graph 2).

If flu prevalence is...	and sensitivity is...	then NPV is...	false-negative rate is...
MODERATE (20%)	POOR (50%)	MODERATE (86%–89%)	MODERATE (11%–14%)
MODERATE (20%)	HIGH (90%)	V. GOOD (97%–99%)	V. LOW (2%–3%)
HIGH (40%)	POOR (50%)	MODERATE (70%–75%)	MODERATE (25%–30%)
HIGH (40%)	HIGH (90%)	V. GOOD (93%–94%)	LOW (6%–7%)

Interpretation of negative results should take into account the clinical characteristics of the case-patient. If an important clinical decision is affected by the test result, the rapid test result should be confirmed by another test, such as viral culture or PCR.

C. Selecting tests

Selection of a test should take into consideration several factors, such as the types of specimens that are considered optimal for that test. Also, tests with high sensitivity and specificity will provide better positive and negative predictive values. Information about test characteristics is provided in product inserts and scientific articles and by the manufacturer.

D. Changes in recommended procedures can affect test results

Modification by the user can affect test performances and increase false-positive and/or false-negative rates. Such modifications include using specimens for which the test is not optimized or using swabs that did not come with the rapid test kit (unless recommended).

E. When are rapid diagnostic tests beneficial?

Use of rapid diagnostic tests are beneficial in these situations:

- To test cases during an outbreak of acute respiratory disease to determine if influenza is the cause, *or*
- To test selected patients during the influenza season, *or*
- In the fall or winter, to test selected patients presenting with respiratory illnesses compatible with influenza to help establish whether influenza is present in a specific population and to guide healthcare providers in diagnosing and treating respiratory illnesses.

In general, the exclusive use of rapid tests does not address the public health need for obtaining viral isolates so that influenza virus strain subtyping and characterization can be conducted to monitor antigenic and genetic changes.

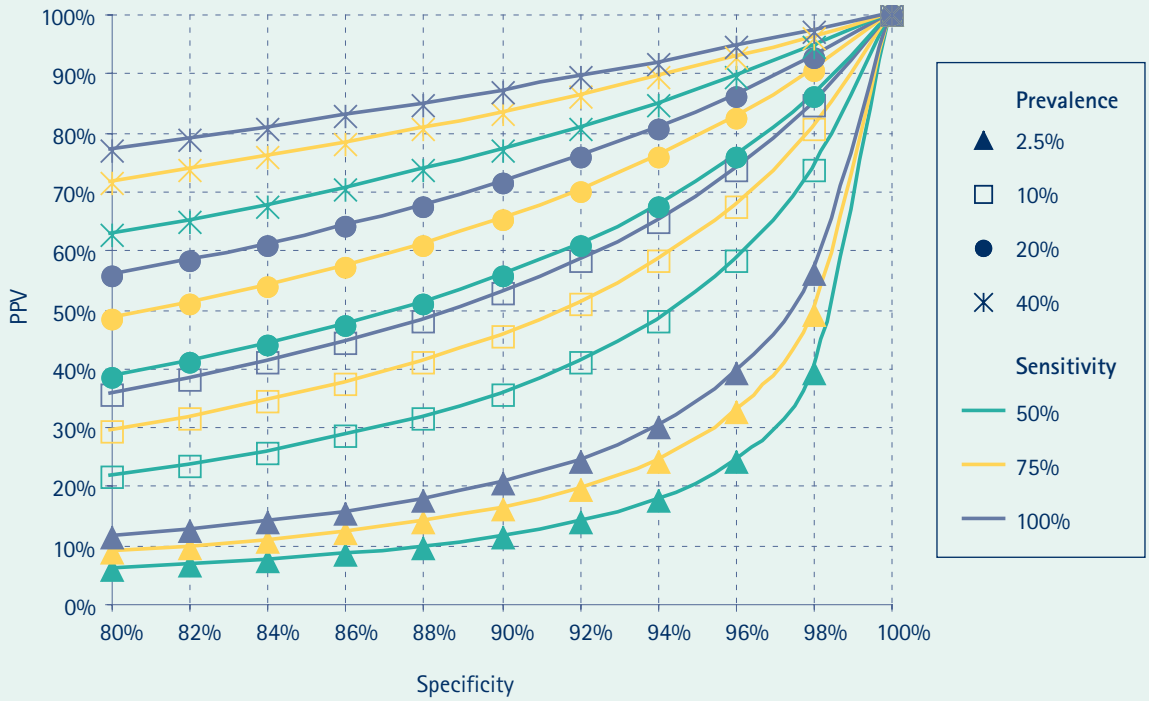
During an influenza pandemic, some rapid diagnostic tests may be able to detect the pandemic strain with adequate sensitivity and specificity. Rapid tests can be used by physicians to supplement clinical diagnoses of pandemic influenza.

> Physicians should be reminded that a negative test result might not rule out influenza and should not affect patient management or infection control decisions.

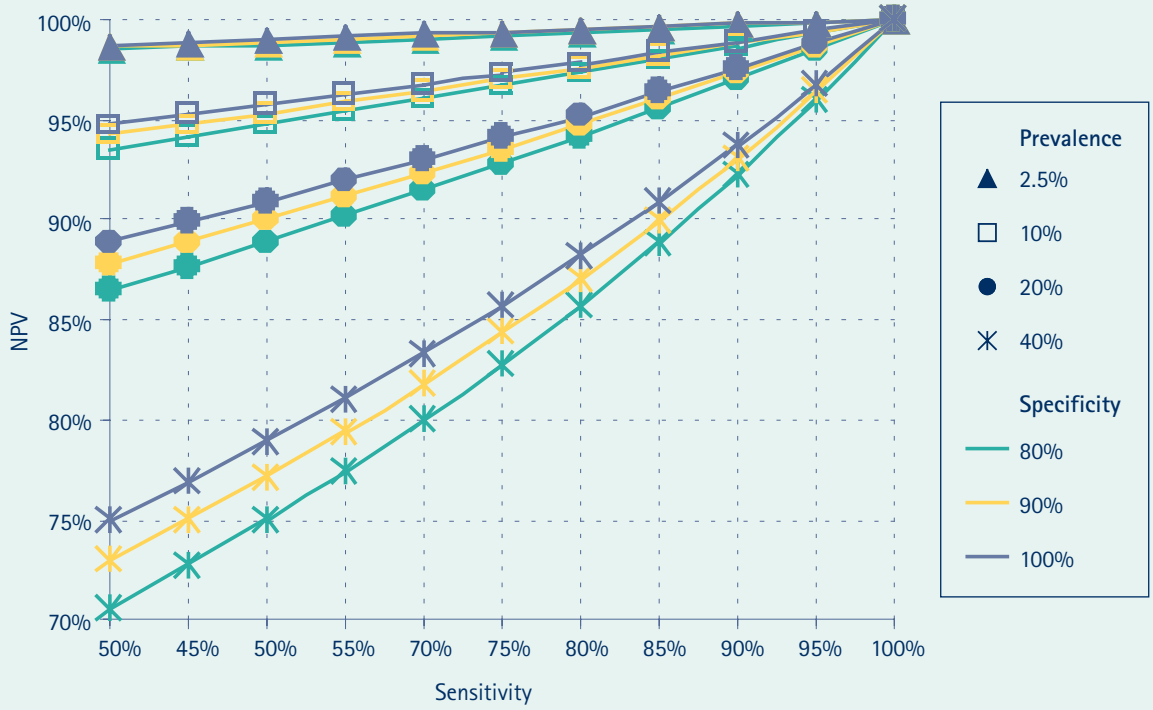
F. For further information

Information on influenza diagnostics is provided on the CDC website at: http://www.cdc.gov/flu/professionals/labdiagnosis.htm.

GRAPH 1: IMPACT OF PREVALENCE, SENSITIVITY AND SPECIFICITY ON POSITIVE PREDICTIVE VALUE



GRAPH 2: IMPACT OF PREVALENCE, SENSITIVITY AND SPECIFICITY ON NEGATIVE PREDICTIVE VALUE



APPENDIX 7. GUIDELINES FOR MEDICAL SURVEILLANCE OF LABORATORY RESEARCH PERSONNEL WORKING WITH NOVEL STRAINS OF INFLUENZA, INCLUDING AVIAN STRAINS AND OTHER STRAINS WITH PANDEMIC POTENTIAL

Key Messages

- Laboratory workers should receive training on the appropriate biosafety level for the type of work being performed.
- Before working with avian influenza A viruses, including highly pathogenic strains, laboratory workers should have a baseline serum sample obtained and stored for future reference.
- Workers in laboratories that contain avian influenza A viruses should report any fever or lower respiratory symptoms to their supervisors. Workers should be evaluated for possible exposures, and the clinical features and course of the illness should be closely monitored.
- Laboratory workers who are believed to have had a laboratory exposure to an avian influenza A virus or other highly pathogenic strain should be evaluated, counseled about the risk of transmission to others, and monitored for fever or lower respiratory symptoms as well as for any of the following: sore throat, rhinorrhea, chills, rigors, myalgia, headache, diarrhea.
- Local and/or state public health departments should be notified promptly of laboratory exposures and illnesses in exposed laboratory workers.

Medical surveillance of laboratory personnel can help to ensure that workers who are at risk of occupational exposure to avian influenza viruses or other novel animal or human influenza strains and who develop symptoms of illness receive appropriate medical evaluation and treatment, both for the benefit of their health and to prevent further transmission.

I. PREREQUISITES FOR WORKING WITH NOVEL AVIAN OR HUMAN INFLUENZA VIRUSES

A. Baseline serum samples

Before working with novel avian or human influenza viruses, laboratory workers should have a baseline serum sample obtained and stored for future reference.

B. Influenza vaccine

Laboratories should offer the current inactivated influenza vaccine to laboratory personnel. Its use is especially encouraged for personnel working with avian viruses in BSL-3 enhanced laboratory conditions and for those who may be exposed to these viruses in the field. Immunization might reduce the chance of illness from exposure to human influenza viruses currently circulating in the community that could lead to confusion in monitoring for avian influenza A infection. Vaccines against novel influenza A viruses (e.g., H5N1) are undergoing clinical trials and might be available in the future.

C. Oseltamivir prophylaxis

- It is not necessary to require oseltamivir for laboratory research personnel working with highly pathogenic influenza strains, but encourage it for those doing animal experiments only for the time they are working with animals and especially while working with ferrets.

- When considering oseltamivir prophylaxis, be sure to evaluate appropriate candidates for contraindications, answer their questions, review adverse effects, and explain the benefits.
- Maintain a log of persons on oseltamivir, persons evaluated and not on oseltamivir, doses dispensed, and adverse effects.
- Periodically evaluate and update oseltamivir policies and procedures.

D. Post-exposure prophylaxis

Conditions for use of oseltamivir for post-exposure prophylaxis include a known or suspected laboratory exposure to live avian influenza virus, including highly pathogenic strains, for a person not on oseltamivir. Appropriate healthcare personnel should be available to evaluate immediately and dispense oseltamivir if the exposure occurs during working hours. If exposure occurs after working hours, an exposed laboratory person should present to the Emergency Department and, after evaluation, communicate with CDC for recommendations.

II. MANAGEMENT OF INFLUENZA-LIKE ILLNESS IN PERSONNEL WITH POSSIBLE EXPOSURE TO NOVEL AVIAN OR HUMAN INFLUENZA VIRUSES

A. General procedures

- Maintain a daily sign-in/out sheet to record name, date, time in/out, use of oseltamivir, and brief description of job tasks. This record will facilitate retrospective documentation if an illness occurs.
- Workers should report any influenza-like illness and any potential laboratory exposures to the supervisor (see also **Supplement 4**).

B. Evaluation and treatment

1. During regular working hours

- The affected employee should notify the supervisor. The supervisor should immediately contact the appropriate healthcare personnel and facility contacts (e.g., occupational health, infection control, or designee).
- Upon arrival at the designated clinic, the employee should be placed in a private room for isolation where a healthcare provider can provide consultation and evaluation.
- The healthcare provider should obtain a respiratory specimen (e.g. nasopharyngeal swab or aspirate) for viral culture. A rapid antigen test[5] with the ability to differentiate between influenza A and B should be used for initial diagnosis, followed by virus isolation.
- Based on: 1) the rapid test result (if influenza A positive), 2) the status of oseltamivir prophylaxis, and 3) the clinical evaluation, the healthcare provider should determine whether the patient will return to work, be sent home, or be sent to an infectious disease consultant.

2. During working hours when the employee calls from home

- The employee should notify the supervisor. The supervisor should discuss the situation with the appropriate healthcare personnel and determine where and by whom the employee will be evaluated and specimens for viral culture will be obtained.

[5] If laboratory capacity is available, RT-PCR should be used to rule out the suspected pathogen.

- The employee may come to an on-site clinic for evaluation or may elect to see a personal physician. If the employee chooses to see a personal physician, the on-site clinician should discuss with the personal physician the likelihood of a laboratory-acquired infection. The personal physician should be asked to collect specimens for antigen detection and viral culture.
- An employee who is not sick enough to be admitted to a hospital should remain at home under the care of a personal physician, pending results from the viral culture. If influenza A (H3N2) or A (H1N1) is identified, the employee should be advised and can resume normal activities as soon as symptoms subside.
- If avian influenza A (e.g., H5, H7, H9) is identified, the family and other contacts should be monitored for illness.[6]
- Local public health officials should be notified about any confirmed avian influenza infections.

3. After working hours

- The employee should notify the supervisor. The supervisor should inform other persons as the situation dictates.
- If the employee is acutely ill with symptoms consistent with influenza, the employee and/or supervisor should contact the appropriate healthcare provider for instructions. The healthcare provider should conduct the initial evaluation and patient management.
- The supervisor should immediately ask the healthcare provider to collect specimens for rapid testing and viral culture.
- The employee should follow the advice of the healthcare provider with regard to further evaluation/treatment.

[6] Persons living with the ill person should be managed as described in Supplement 4.

supplement 3 healthcare planning

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SUMMARY OF ROLES AND RESPONSIBILITIES FOR HEALTHCARE AND PUBLIC HEALTH PARTNERS

INTERPANDEMIC AND PANDEMIC ALERT PERIODS

Healthcare facility responsibilities:

- Develop planning and decision-making structures for responding to pandemic influenza.
- Develop written plans that address: disease surveillance, hospital communications, education and training, triage and clinical evaluation, facility access, occupational health, use and administration of vaccines and antiviral drugs, surge capacity, supply chain and access to critical inventory needs, and mortuary issues.
- Participate in pandemic influenza response exercises and drills, and incorporate lessons learned into response plans.

State and local responsibilities:

- Develop statewide and local or regional plans to manage an influenza pandemic.
- Assist healthcare facilities in conducting exercises and drills to test healthcare response issues and build partnerships among healthcare and public health officials, community leaders, and emergency response workers.
- Develop a communications infrastructure to facilitate and ensure the timely dissemination and transfer of information between the healthcare and public health sectors.
- Address legal issues that can affect staffing and patient care.

HHS responsibilities:

- Provide ongoing public health guidance on healthcare preparedness for an influenza pandemic.
- Provide healthcare facilities with model protocols for early detection and treatment of influenza among patients and staff; these protocols can be piloted during routine influenza seasons.

PANDEMIC PERIOD

If an influenza pandemic begins in another country:

Healthcare facility responsibilities:

- Heighten institutional surveillance for influenza and prepare to activate institutional pandemic influenza plans, as necessary.

State and local responsibilities:

- Work with HHS to provide local physicians and hospital administrators with updated information and guidance as the situation unfolds.

PANDEMIC PERIOD (CONT.)

If an influenza epidemic begins in or enters the United States:

Healthcare facility responsibilities:

- Activate institutional pandemic influenza plans, in accordance with the "Hospital Pandemic Influenza Triggers" outlined in Table 1.
- Identify and isolate all potential patients with pandemic influenza.
  - Implement infection control practices to prevent influenza transmission.
  - Ensure rapid and frequent communication within healthcare facilities and between healthcare facilities and health departments.
- Implement surge-capacity plans to sustain healthcare delivery.

State and local health responsibilities:

- Provide healthcare facilities with information on the global, national, and local situation.
- Work with HHS to provide guidance (as needed) on infection control measures for healthcare and non-healthcare settings.
- Work with healthcare facilities to address surge capacity needs.

HHS responsibilities:

- Assist state and local healthcare and public health partners on issues related to hospital infection control, occupational health, antiviral drug use and clinical management, vaccination, and medical surge capacity.
- Provide states with materials from the Strategic National Stockpile for further distribution to healthcare facilities.

S3-I. RATIONALE

An influenza pandemic will place a huge burden on the U.S. healthcare system. Published estimates based on extrapolation of the 1957 and 1968 pandemics suggest that there could be 839,000 to 9,625,000 hospitalizations, 18–42 million outpatient visits, and 20–47 million additional illnesses, depending on the attack rate of infection during the pandemic.[1] Estimates based on extrapolation from the more severe 1918 pandemic suggest that substantially more hospitalizations and deaths could occur. The demand for inpatient and intensive-care unit (ICU) beds and assisted ventilation services could increase by more than 25% under the less severe scenario. Pre-pandemic planning by healthcare facilities is therefore essential to provide quality, uninterrupted care to ill persons and to prevent further spread of infection. Effective planning and implementation will depend on close collaboration among state and local health departments,[2] community partners, and neighboring and regional healthcare facilities. Despite planning and preparedness, however, in a severe pandemic it is possible that shortages, for example of mechanical ventilators, will occur and medical care standards may need to be adjusted to most effectively provide care and save as many lives as possible.

1 Meltzer et al, EID 2004 Meltzer MI, Cox NJ, Fukuda K The economic impact of pandemic influenza in the United States: priorities for intervention. EID 1999 Sep-Oct;5(5):659-71.

2 Depending on the locality, health departments may also include territorial or tribal health departments.

S3-II. OVERVIEW

Supplement 3 provides healthcare partners with recommendations for developing plans to respond to an influenza pandemic. The focus is on planning during the Interpandemic Period for: pandemic influenza surveillance, decision-making structures for responding to a pandemic, hospital communications, education and training, patient triage, clinical evaluation and admission, facility access, occupational health, distribution of vaccines and antiviral drugs, surge capacity, and mortuary issues. Planning for the provision of care in non-hospital settings—including residential care facilities, physicians' offices, private home healthcare services, emergency medical services, federally qualified health centers (FQHCs),[3] rural health clinics, and alternative care sites—is also addressed.

The recommendations for the Pandemic Period focus on activation of institutional pandemic influenza response plans. The ability to provide detailed guidance on this aspect of the pandemic is limited because of uncertainty about how the pandemic will evolve and variation and uncertainty of local factors that will influence decisions at various stages.

The activities suggested in **Supplement 3** are intended to be synergistic with those of other pandemic influenza planning efforts, including state preparedness plans. Links to additional resources that provide the most up-to-date guidance on particular topics are included. A checklist to help facilities assess their current level of readiness to deal locally with an influenza pandemic is provided in Appendix 2.

S3-III. RECOMMENDATIONS FOR THE INTERPANDEMIC AND PANDEMIC ALERT PERIODS

A. Planning for provision of care in hospitals

U.S. healthcare facilities must be prepared for the rapid pace and dynamic characteristics of pandemic influenza. All hospitals should be equipped and ready to care for: 1) a limited number of patients infected with a pandemic influenza virus, or other novel strains of influenza, as part of normal operations; and 2) a large number of patients in the event of escalating transmission of pandemic influenza.

Hospital response plans for pandemic influenza should:

- Outline administrative measures for detecting the introduction of pandemic influenza, preventing its spread, and managing its impact on the facility and the staff.
- Build on existing preparedness and response plans for bioterrorism events, SARS, and other infectious disease emergencies.
- Incorporate planning suggestions from state and local health departments and other local and regional healthcare facilities and response partners.
- Identify criteria and methods for measuring compliance with response measures (e.g., infection control practices, case reporting, patient placement, healthcare worker illness surveillance).
- Review and update inventories of supplies that will be in high demand during an influenza pandemic.
- Review procedures for the receipt, storage, and distribution of assets received from federal stockpiles.
- Include mechanisms for periodic reviews and updates.

3 A federally qualified health center (FQHC) is a type of provider defined by the Medicare and Medicaid statutes. FQHCs include health centers receiving grants under section 330 of the Public Health Service Act, certain tribal organizations, and clinics designated by HHS as FQHC Look-Alikes. More information may be found at: http://www.cms.hhs.gov/providers/fqhc/

Hospitals that intend to use an "all-hazards" incident command structure for responding to pandemic influenza will need to incorporate the relevant aspects of communicable disease control that are included in this supplement and in **Supplement 4**. Hospitals should consider using "table top" simulations or other exercises to test response capabilities (see Appendix 1).

1. Planning process

- Groups and individuals involved in the hospital planning process should include:
  - An internal, multidisciplinary planning committee with responsibility for pandemic influenza preparedness and response. The committee should include technical experts, persons with decision-making authority, and representatives from a range of response partners (see Box 1). A pre-existing all-hazards preparedness team (e.g., established for bioterrorism or SARS response) might assume this role.
  - A response coordinator/incident commander to direct the facility's planning and response efforts
  - A core group from the multidisciplinary planning committee to work with the response coordinator and assist with decision-making during the pandemic
- The pandemic influenza response team should plan to remain active throughout the pandemic period, which could be several weeks or months.
- Hospital planning for pandemic influenza should consider concurrent public health, community, and healthcare planning efforts at the local, state, and regional levels. Some possible mechanisms for collaboration and coordination are to:
  - Include a state or local health department representative as an ex officio member on the hospital planning committee (see Box 1).
  - Obtain copies of draft pandemic influenza plans from other local or regional hospitals to use as models.
  - Work with other local hospitals, community organizations (e.g., social service groups), and the state or local health department to coordinate healthcare activities in the community and define responsibilities for each entity during a pandemic.
  - Collaborate with HRSA hospital preparedness programs in the state or region.
  - Include a hospital representative in local or regional planning efforts.
  - Include representatives from safety-net providers[4] in the local community (e.g., FQHCs and rural health clinics).

2. Planning elements

The elements of a hospital influenza pandemic preparedness plan discussed below are listed in the Hospital Preparedness Checklist provided in Appendix 2.

a) Hospital surveillance

- **Hospital surveillance for novel strains of influenza**
  During the Interpandemic and Pandemic Alert Periods, healthcare providers and healthcare facilities play an essential role in surveillance for suspected cases of infection with novel strains of influenza and should be on the alert for such cases. Novel strains may include avian or animal influenza strains that can infect humans (like avian influenza A

4 Health care safety net providers deliver care to low-income and other vulnerable populations, including the uninsured and those covered by Medicaid. Many of these providers have either a legal mandate or an explicit policy to provide services regardless of a patient's ability to pay (http://www.ahcpr.gov/data/safetynet/faq.htm). Major safety net providers include public hospitals and community health centers as well as teaching and community hospitals, and private physicians.

[H5N1]) and new or re-emergent human viruses that cause cases or clusters of human disease. For detection of cases during the Interpandemic and Pandemic Alert Periods, hospitals should have:

- Procedures in place to facilitate laboratory testing on-site using proper biosafety levels and reporting of unusual influenza isolates through local and state health department channels (see **Supplement 1**). If appropriate methods or biosafety levels do not exist at the hospital, specimens should be shipped to the state health department.
- Predetermined thresholds for activating pandemic influenza surveillance plans (see S3-III.A and the Table).

- **Hospital surveillance for pandemic influenza**
  During the Pandemic Period, healthcare providers and healthcare facilities will play an essential role in pandemic influenza surveillance (see **Supplement 1**). For detection of cases during the Pandemic Period, hospitals should have:
  - Mechanisms for conducting surveillance in emergency departments to detect any increases in influenza-like illness (see box below) during the early stages of the pandemic
  - Mechanisms for monitoring employee absenteeism for increases that might indicate early cases of pandemic influenza
  - Mechanisms for tracking emergency department visits and hospital admissions and discharge of suspected or laboratory-confirmed pandemic influenza patients. This information will be needed to: 1) support local public health personnel in monitoring the progress and impact of the pandemic, 2) assess bed capacity and staffing needs, and 3) detect a resurgence in pandemic influenza that might follow the first wave of cases.
  - Updated information on the types of data that should be reported to state or local health departments (e.g., admissions; discharges/deaths; patient characteristics such as age, underlying disease, and secondary complications; illnesses in healthcare personnel) and plans for how these data will be collected during a pandemic. State and local health departments will provide guidance on the scope and mechanism of reporting (see **Supplement 1**).
  - Criteria for distinguishing pandemic influenza from other respiratory diseases (see **Supplement 5**).

Symptoms of influenza include fever, headache, myalgia, prostration, coryza, sore throat, and cough. Nausea and vomiting are also commonly reported among children. Typical influenza (or "flu-like") symptoms, such as fever, may not always be present in elderly patients, young children, patients in long-term care facilities, or persons with underlying chronic illnesses (see **Supplement 5**, Box 2).

b) Hospital communications

Each hospital should work with public health officials, other government officials, neighboring healthcare facilities, the lay public, and the press to ensure rapid and ongoing information-sharing during an influenza pandemic.

- **External communications**
  - Assign responsibility for external communication about pandemic influenza; identify a person responsible for updating public health reporting (e.g., infection control), a clinical spokesperson (e.g., medical director), and a media spokesperson (e.g., public information officer).
  - Identify points of contact among local media (e.g., newspaper, radio, television) representatives and public officials and community leaders.
  - With guidance from state or local health departments, determine the methods, frequency, and scope of external communications.
  - Determine how communications between local and regional healthcare facilities will be handled.

- Consult with state or local health departments on plans for coordinating or facilitating communication among healthcare facilities. In the absence of such a plan, consider organizing a meeting of local health facilities to determine an optimal communications strategy.
- Identify key topics for ongoing communication (e.g., staffing needs, bed capacity, durable and consumable medical equipment and device needs, supplies of influenza vaccine and antiviral drugs).
- Assign responsibility within the hospital for communications with other healthcare facilities.

- Consult with local or state public health officials regarding the hospital's role in communicating with the media and the public.
- Determine the type of hospital-specific communications (e.g., press releases, community bulletin board) that might be needed, and develop templates for these materials.
- Consult with local or state health departments on plans for a pandemic influenza hotline and/or website for public inquiries.
  - Determine how public inquiries will be handled (e.g., refer callers to the health department; provide technical support for handling calls).
  - Identify the types of information that will be provided by the hospital and the types of inquiries that will be referred to state or local health departments.

- **Internal communications**
  - Determine how to keep administrators, personnel (including infection control staff and intake and triage staff), patients, and visitors informed of the ongoing impact of pandemic influenza on the facility and on the community.

c) Education and training

Each hospital should develop an education and training plan that addresses the needs of staff, patients, family members, and visitors. Hospitals should assign responsibility for coordination of the pandemic influenza education and training program and identify training materials—in different languages and at different reading levels, as needed—from HHS agencies, state and local health departments, and professional associations (see Appendix 1).

- **Staff Education**
  - Identify educational resources for clinicians, including federally sponsored teleconferences, state and local health department programs, web-based training materials, and locally prepared presentations.
  - General topics for staff education should include:
    - Prevention and control of influenza
    - Implications of pandemic influenza
    - Benefits of annual influenza vaccination
    - Role of antiviral drugs in preventing disease and reducing rates of severe influenza and its complications
    - Infection control strategies for the control of influenza, including respiratory hygiene/cough etiquette, hand hygiene, standard precautions, droplet precautions, and, as appropriate, airborne precautions (see **Supplement 4**).
  - Hospital-specific topics for staff education should include:
    - Policies and procedures for the care of pandemic influenza patients, including how and where pandemic influenza patients will be cohorted
    - Pandemic staffing contingency plans, including how the facility will deal with illness in personnel

- Policies for restricting visitors and mechanisms for enforcing these policies
- Reporting to the health department suspected cases of infection caused by novel influenza strains during the Interpandemic and Pandemic Alert Periods
- Measures to protect family and other close contacts from secondary occupational exposure

- Establish a schedule for training/education of clinical staff and a mechanism for documenting participation. Consider using annual infection control updates/meetings, medical Grand Rounds, and other educational venues as opportunities for training on pandemic influenza.
- Cross-train clinical personnel, including outpatient healthcare providers, who can provide support for essential patient-care areas (e.g., emergency department, ICU, medical units).
- Train intake and triage staff to detect patients with influenza symptoms and to implement immediate containment measures to prevent transmission (see also **Supplement 5)**.
- Supply social workers, psychologists, psychiatrists, and nurses with guidance for providing psychological support to patients and hospital personnel during an influenza pandemic (see **Supplement 11**). (HHS agencies will identify or develop educational materials on: signs of distress, traumatic grief, stress management and effective coping strategies, building and sustaining personal resilience, and behavioral and psychological support resources.) If feasible, hospitals should also provide psychological-support training to appropriate individuals who are not mental health professionals (e.g., primary-care clinicians, leaders of community and faith-based organizations).
- Develop a strategy for "just-in-time" training of non-clinical staff who might be asked to assist clinical personnel (e.g., help with triage, distribute food trays, transport patients), students, retired health professionals, and volunteers who might be asked to provide basic nursing care (e.g., bathing, monitoring of vital signs); and other potential in-hospital caregivers (e.g., family members of patients).

- **Education of patients, family members, and visitors**
  Patients and others should know what they can do to prevent disease transmission in the hospital, as well as at home and in community settings.
  - Identify language-specific and reading-level appropriate materials for educating patients, family members, and hospital visitors during an influenza pandemic. If language-specific materials are not available for the population(s) being served, arrange for translations.
  - Develop a plan for distributing information to all persons who enter the hospital. Identify staff to answer questions about procedures for preventing influenza transmission.

d) Triage, clinical evaluation, and admission procedures

During the peak of a pandemic, hospital emergency departments and outpatient offices might be overwhelmed with patients seeking care. Therefore, triage should be conducted to: 1) identify persons who might have pandemic influenza, 2) separate them from others to reduce the risk of disease transmission, and 3) identify the type of care they require (i.e., home care or hospitalization) (see **Supplement 5**).

- Develop a strategy for triage, diagnosis, and isolation of possible pandemic influenza patients. Consider the following triage mechanisms:
  - Using phone triage to identify patients who need emergency care and those who can be referred to a medical office or other non-urgent facility
  - Assigning separate waiting areas for persons with respiratory symptoms
  - Assigning a separate triage evaluation area for persons with respiratory symptoms

- Assigning a "triage coordinator" to manage patient flow, including deferring or referring patients who do not require emergency care (see **Supplement 4** and **Supplement 5**).

- Review procedures for the clinical evaluation of patients in the emergency department and in outpatient medical offices to facilitate efficient and appropriate disposition of patients.
- Review admission procedures and streamline them as needed to limit the number of patient encounters in the hospital (e.g., direct admission to an inpatient bed).
- Identify a "trigger" point at which screening for signs and symptoms of pandemic influenza in all persons entering the hospital will escalate from passive (e.g., signs at the entrance) to active (e.g., direct questioning). In addition to visual alerts, potential screening measures might include priority triage of persons with respiratory symptoms and telephone screening of patients with appointments.

e) Facility access

Hospitals should determine in advance the criteria and procedures they will use to limit access to the facility if pandemic influenza spreads through the community.

- Define "essential" and "non-essential" visitors with regard to the hospital and the population served. Develop protocols for limiting non-essential visitors.
- Develop criteria or "triggers" for temporary closing of the hospital to new admissions and transfers. The criteria should consider staffing ratios, isolation capacity, and risks to non-influenza patients. As part of this effort, hospital administrators should: 1) determine who will make decisions about temporary closings and how and to whom these decisions will be communicated, and 2) consult with state and local health departments on their roles in determining policies for hospital admissions and transfers.
- Determine how to involve hospital security services in enforcing access controls. Consider meeting with local law enforcement officials in advance to determine what assistance, if any, they can provide. Note that local law enforcement might be overburdened during a pandemic and have limited ability to assist healthcare facilities with security services.

f) Occupational health

The ability to deliver quality health care is dependent on adequate staffing and optimum health and welfare of staff. During a pandemic,[5] the healthcare workforce will be stressed physically and psychologically. Like others in the community, many healthcare workers will become ill. Healthcare facilities must be prepared to: 1) protect healthy workers from exposures in the healthcare setting through the use of recommended infection control measures; 2) evaluate and manage symptomatic and ill healthcare personnel; 3) distribute and administer antiviral drugs and/or vaccines to healthcare personnel, as recommended by HHS and state health departments; and 4) provide psychosocial services to health care workers and their families to help sustain the workforce.

- **Managing ill workers**
  - Establish a plan for detecting signs and symptoms of influenza in healthcare personnel before they report for duty.
  - Develop policies for managing healthcare workers with respiratory symptoms that take into account HHS recommendations for healthcare workers with influenza (see www.cdc.gov/ncidod/hip/GUIDE/infectcont98.htm
  - Consider assigning staff who are recovering from influenza to care for influenza patients.

[5] During the Pandemic Alert Period, healthcare personnel exposed to avian influenza A (H5N1) or other novel strains of influenza should be managed on a case-by-case basis (see **Supplement 5**).

- **Time-off policies**
  Ensure that time-off policies and procedures consider staffing needs during periods of clinical crisis.
- **Reassignment of high-risk personnel**
  Establish a plan to protect personnel at high risk for complications of influenza (e.g., pregnant women, immunocompromised persons) by reassigning them to low-risk duties (e.g., non-influenza patient care, administrative duties that do not involve patient care) or placing them on furlough.
- **Psychosocial health services** (see also **Supplement 11**)
  - Identify mental health and faith-based resources for counseling of healthcare personnel during a pandemic. Counseling should include measures to maximize professional performance and personal resilience by addressing management of grief, exhaustion, anger, and fear; physical and mental health care for oneself and one's loved ones; and resolution of ethical dilemmas.
  - Determine a strategy for supporting healthcare workers' needs for rest and recuperation.
  - Develop a strategy for housing and feeding healthcare personnel who might be needed on-site for prolonged periods
  - Develop a strategy for accommodating and supporting staff who have child- or elder-care responsibilities.
- **Influenza vaccination and use of antiviral drugs**
  - Promote annual influenza vaccination among hospital employees. Increased vaccination coverage during the Interpandemic Period might help increase vaccine acceptance during a pandemic and will limit the spread of seasonal influenza.
  - Ensure that a system is in place for documenting influenza vaccination of healthcare personnel. The hospital might decide to enroll in the National Healthcare Safety Network (NHSN; www.cdc.gov/ncidod/hip/NNIS/members/nhsn.htm) to help track employee vaccination and health status.
  - Establish a strategy for rapidly vaccinating or providing antiviral prophylaxis or treatment to healthcare personnel as recommended by HHS and state health departments. Preliminary recommendations on the use of antiviral drugs and vaccination have been established (see **Part 1, Appendix E** and **Supplement 6** and **Supplement 7**) but will need to be tailored to fit the epidemiology of the pandemic.

g) Use and administration of vaccines and antiviral drugs

- **Pandemic influenza vaccine and "pre-pandemic" influenza vaccine**
  Once the characteristics of a new pandemic influenza virus are identified, the development of a pandemic vaccine will begin. Recognizing that there may be benefits to immunization with a vaccine prepared before the pandemic against an influenza virus of the same subtype, efforts are underway to stockpile vaccines for subtypes with pandemic potential. As supplies of these vaccines become available, it is possible that some healthcare personnel and others critical to a pandemic response will be recommended for vaccination to provide partial protection or immunological priming for a pandemic strain. Policies for the use of pre-pandemic vaccine have not been finalized.
- Interim recommendations on priority groups for vaccination and strategies for vaccine distribution are discussed in **Supplement 6**. During a pandemic, these recommendations will be updated, taking into account populations which are most at risk. In the interim, healthcare facilities should:
  - Monitor updated HHS information and recommendations on the development, distribution, and use of a pandemic influenza vaccine (http://www.pandemicflu.gov)
  - Work with local and state health departments on plans for distributing pandemic influenza vaccine.
  - Provide estimates of the quantities of vaccine needed for hospital staff and patients, as requested by the state health department.

- Develop a stratification scheme for prioritizing vaccination of healthcare personnel who are most critical for patient care and essential personnel to maintain the day-to-day operation of the healthcare facility.
- Develop a pandemic influenza vaccination plan in the hospital.

- **Antiviral drugs**
  Antiviral drugs effective against the circulating pandemic strain can be used for treatment and possibly prophylaxis during an influenza pandemic. Because of the effectiveness of treatment with antiviral drugs such as oseltamivir and zanamivir, and the greater efficiency of treatment in a setting of limited supply, the use of prophylaxis will be restricted to maximize health benefits. Interim recommendations for the use of antiviral drugs are discussed in **Supplement 7**. Healthcare facilities should consider how antiviral drugs might be used in their patient and healthcare worker populations, taking into account state and national guidelines, and determine if a reserve supply should be stockpiled. (See also HRSA cooperative agreements www.hrsa.gov/grants/preview/guidancespecial/hrsa05001.htm.)

h) Surge capacity

Healthcare facilities should plan ahead to address emergency staffing needs and increased demand for isolation wards, ICUs, assisted ventilation services, and consumable and durable medical supplies (Box 2). Hospital planners can use FluSurge software (http://www.cdc.gov/flu/flusurge.htm) to estimate the potential impact of a pandemic on resources such as staffed beds (both overall and ICU) and ventilators (see also HRSA and AHRQ planning and surge capacity resources listed in Appendix 1.)

- **Staffing**
  - Assign responsibility for the assessment and coordination of staffing during an emergency.
  - Estimate the minimum number and categories of personnel needed to care for a single patient or a small group of patients with influenza complications on a given day.
  - Determine how the hospital will meet staffing needs as the number of patients with pandemic influenza increases and/or healthcare and support personnel become ill or remain at home to care for ill family members. Consider the following options:
    - Assigning patient-care responsibilities to clinical administrators
    - Recruiting retired healthcare personnel
    - Using trainees (e.g., medical and nursing students)
    - Using patients' family members in an ancillary healthcare capacity
  - Collaborate with local and regional healthcare-planning groups in an attempt to achieve adequate staffing of the hospital during an influenza pandemic (e.g., decide whether and how staff will be shared with other healthcare facilities, determine how salary issues will be addressed for employees shared between facilities, and consider ways to increase the number of home healthcare staff to reduce hospital admissions during the emergency). State and local health departments can help assess the feasibility of recruiting staff from different hospitals and/or regions, working in coordination with federal facilities, including Veterans Administration and Department of Defense hospitals. Healthcare facilities may implement these arrangements through Mutual Aid Agreements (MAAs) or Memoranda of Understanding/Agreement (MOU/As).
  - Increase cross-training of personnel to provide support for essential patient-care areas at times of severe staffing shortages (e.g., in emergency departments, ICUs, or medical units) (see also S3-III.A.2.c).
  - Create a list of essential-support personnel titles (e.g., environmental and engineering services, nutrition and food services, administrative, clerical, medical records, information technology, laboratory) that are needed to maintain hospital operations.

- Create a list of non-essential positions that can be re-assigned to support critical hospital services or placed on administrative leave to limit the number of persons in the hospital.
- Consult with the state health department[6] on plans for rapidly credentialing healthcare professionals during a pandemic. This might include defining when an "emergency staffing crisis" can be declared and identifying emergency laws that allow employment of healthcare personnel with out-of-state licenses.
- Identify insurance and liability issues related to the use of non-facility staff.
- Explore opportunities for recruiting healthcare personnel from other healthcare settings, (e.g., medical offices and day-surgery centers). Consult public health partners about existing state or local plans for recruitment and deployment of local personnel.

- **Bed capacity**
  - Review and revise admissions criteria for times when bed capacity is limited (see also S3-III.A.2.e).
  - Develop policies and procedures for expediting the discharge of patients who do not require ongoing inpatient care (e.g., develop plans and policies for transporting discharged patients home or to other facilities; create a patient discharge holding area or discharge lounge to free up bed space).
  - Work with home healthcare agencies to arrange at-home follow-up care for patients who have been discharged early and for those whose admission was deferred because of limited bed space.
  - Develop criteria or "triggers" for temporarily canceling elective surgical procedures and determining what and where emergency procedures will be performed during a pandemic. Determine which elective procedures will be temporarily postponed.
  - Determine whether patients who require emergency procedures will be transferred to another hospital.
  - Discuss with local and state health departments how bed availability, including available ICU beds and ventilators, will be tracked during a pandemic.
  - Consult with hospital licensing agencies on plans and processes to expand bed capacity during times of crisis. These efforts should take into account the need to provide staff and medical equipment and supplies to care for the occupant of each additional hospital bed.
  - Discuss with healthcare regulators whether, how, and when an "Altered Standards of Care in Mass Casualty Events" will be invoked and applied to pandemic influenza (See http://www.ahrq.gov/research/altstand/).
  - Develop policies and procedures for shifting patients between nursing units to free up bed space in critical-care areas and/or to cohort pandemic influenza patients.
  - Develop Mutual Aid Agreements (MAAs) or Memoranda of Understanding/Agreement (MOU/As) with other local facilities who can accept non-influenza patients who do not need critical care.
  - Identify areas of the facility that could be vacated for use in cohorting influenza patients. Consider developing criteria for shifting use of available space based on ability to support patient-care needs (e.g., access to bathroom and shower facilities). Consider developing cohorting protocols based on a patient's stage of recovery and infectivity.

- **Consumable and durable supplies**
  - Evaluate the existing system for tracking available medical supplies in the hospital to determine whether it can detect rapid consumption, including items that provide personal protection (e.g., gloves, masks). Improve the system as

6 The HRSA Emergency System for Advance Registration of Volunteer Health Professionals (ESAR-VHP) is helping each state and territory establish a standardized volunteer registration system. Additional information is available at: www.hrsa.gov/bioterrorism/esarvhp/. Two new draft standards on emergency credentialing have been offered for public comment by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO; http://www.jcaho.org/).

needed to respond to growing demands for resources during an influenza pandemic (http://www.cdc.gov/flu/flusurge.htm).

- Consider stockpiling enough consumable resources such as masks (see Box 2) for the duration of a pandemic wave (6-8 weeks).
- Assess anticipated needs for consumable and durable resources, and determine a trigger point for ordering extra resources. Estimate the need for respiratory care equipment (including mechanical ventilators), and develop a strategy for acquiring additional equipment if needed. Neighboring hospitals might consider developing inventories of equipment and determining whether and how that equipment might be shared during a pandemic.
- Anticipate needs for antibiotics to treat bacterial complications of influenza, and determine how supplies can be maintained during a pandemic (see **Supplement 5**).
- Establish contingency plans for situations in which primary sources of medical supplies become limited. Consult with the local and state health departments about access to the national stockpile during an emergency.

- **Continuation of essential medical services**
  - Address how essential medical services will be maintained for persons with chronic medical problems served by the hospital (e.g., hemodialysis patients).
  - Develop a strategy for ensuring uninterrupted provision of medicines to patients who might not be able to (or should not) travel to hospital pharmacies.

i) Security

Healthcare facilities should plan for additional security. This may be required given the increased demand for services and possibility of long wait times for care, and because triage or treatment decisions may lead to people not receiving the care they think they require.

j) Mortuary issues

To prepare for the possibility of mass fatalities during an influenza pandemic, hospitals should do the following:

- Assess current capacity for refrigeration of deceased persons.
- Discuss mass fatality plans with local and state health officials and medical examiners.
- Work with local health officials and medical examiners to identify temporary morgue sites.
- Determine the scope and volume of supplies (e.g., body bags) needed to handle an increased number of deceased persons.

Resources for addressing these issues are provided in Appendix 1.

B. Planning for provision of care in non-hospital settings

Planning and effective delivery of care in outpatient settings is critical. Appropriate management of outpatient influenza cases will reduce progression to severe disease and thereby reduce demand for inpatient care. A system of effective outpatient management will have several components. To decrease the burden on providers and to lessen exposure of the "worried well" to persons with influenza, telephone hotlines should be established to provide advice on whether to stay home or to seek care. Most persons who seek care can be managed appropriately by outpatient providers. Health care networks may designate specific providers, offices, or clinics for patients with influenza-like illness. Nevertheless, some persons with influenza will likely present to all medical offices and clinics so that planning and preparedness is important at every outpatient care site. In underserved areas, health departments may establish influenza clinics to facilitate access. Hospitals should develop a strategy for triage of potential influenza patients, which may include establishing a site outside of the Emergency Department

where persons can be seen initially and identified as needing emergency care or may be referred to an outpatient care site for diagnosis and management. Finally, home health care providers and organizations can provide follow-up for those managed at home, decreasing potential exposure of the public to persons who are ill and may transmit infection

Effective management of outpatient care in communities will require that health departments, health care organizations, and providers communicate and plan together. Issues to address include:

- Plan to establish and staff telephone hotlines.
- Develop training modules, protocols and algorithms for hotline staff.
- Within health care networks, develop plans on the organization of care for influenza patients and develop materials and strategies to inform patients on care-seeking during a pandemic
- For clinics and offices, develop plans that include education, staffing, triage, infection control in waiting rooms and other areas, and communication with healthcare partners and public health authorities.

1. Non-hospital healthcare facilities

The hospital planning recommendations (see S3-III.A) can serve as a model for planning in other healthcare settings, including nursing homes and other residential care facilities, and primary care health centers. All healthcare facilities should do the following:

- Create a planning team and develop a written plan.
- Establish a decision-making and coordinating structure that can be tested during the Interpandemic Period and will be activated during an influenza pandemic.
- Determine how to conduct surveillance for pandemic influenza in healthcare personnel and, for residential facilities, in the population served.
- Develop policies and procedures for managing pandemic influenza in patients and staff.
- Educate and train healthcare personnel on pandemic influenza and the healthcare facility's response plan.
- Determine how the facility will communicate and coordinate with healthcare partners and public health authorities during a pandemic.
- Determine how the facility will communicate with patients and help educate the public regarding prevention and control measures.
- Develop a plan for procuring the supplies (e.g., personal protective equipment [PPE]) needed to manage influenza patients.
- Determine how the facility will participate in the community plan for distributing either vaccine or antiviral drugs, including possibly serving as a point of distribution and providing staff for alternative community points of distribution.

Emergency medical services, private homecare services, FQHCs, and rural health clinics may adapt their planning activities from this model. In some parts of the country, FQHCs and rural health clinics may need to rely on volunteers[7] to provide and administer pandemic influenza vaccines.

2. Alternative care sites

If an influenza pandemic causes severe illness in large numbers of people, hospital capacity might be overwhelmed. In that

7 As mentioned in footnote #6, the HRSA Emergency System for Advance Registration of Volunteer Health Professionals (ESAR-VHP) is helping each state and territory establish a standardized volunteer registration system. Additional information is available at: www.hrsa.gov/bioterrorism/esarvhp/.

case, communities will need to provide care in alternative sites (e.g., school gymnasiums, armories, convention centers). (Also see http://www.ahrq.gov/research/altsites.htm.) The selection of alternative care sites for pandemic influenza should specifically address the following infection control and patient care needs:

- Bed capacity and spatial separation of patients
- Facilities and supplies for hand hygiene
- Lavatory and shower capacity for large numbers of patients
- Food services (refrigeration, food handling, and preparation)
- Medical services
- Staffing for patient care and support services
- PPE supplies
- Cleaning/disinfection supplies
- Environmental services (linen, laundry, waste)
- Safety and Security

S3-IV. RECOMMENDATIONS FOR THE PANDEMIC PERIOD

A. Activating the facility's pandemic influenza response plan

Following initial detection of pandemic influenza anywhere in the world, the facility's pandemic influenza response plan should be activated in accordance with the level of pandemic activity (see Table).

1. Pandemic influenza reported outside the United States

If cases of pandemic influenza have been reported outside the United States, the main steps will be to:

- Establish contact with key public health, healthcare, and community partners.
- Implement hospital surveillance for pandemic influenza, including detection of patients admitted for other reasons who might be infected with the pandemic strain of influenza virus.
- Implement a system for early detection and antiviral treatment of healthcare workers who might be infected with the pandemic strain of influenza virus.
- Reinforce infection control measures to prevent the spread of influenza (see S5-IV.B and **Supplement 4**).
- Accelerate the training of staff, in accordance with the facility's pandemic influenza education and training plan.

2. Pandemic influenza reported in the United States

If cases of pandemic influenza have been reported in the United States, additional steps will be to:

- Identify when pandemic influenza cases begin in the community. See also **Supplement 1**.
- Identify, isolate, and treat all patients with potential pandemic influenza. See also **Supplements 4, 5, and 8**.
- Implement activities to increase capacity, supplement staff shortages, and provide supplies and equipment.
- Maintain close communication within and among healthcare facilities and with state and local health departments.

BOX 1. HEALTHCARE FACILITY PANDEMIC INFLUENZA PLANNING COMMITTEE

Representatives for a hospital pandemic influenza planning committee may include:

- **Hospital staff**
  - Administration/senior management (including fiscal officer)
  - Legal counsel/risk management
  - Infection control/hospital epidemiology
  - Hospital disaster/emergency coordinator
  - Engineering/physical plant/industrial hygiene/institutional safety
  - Nursing administration
  - Medical staff (including outpatient areas)
  - Intensive-care unit
  - Emergency department
  - Laboratory services
  - Respiratory therapy
  - Nutrition and food services
  - Pharmacy
  - Environmental services (housekeeping, laundry)
  - Public relations
  - Security
  - Materials management
  - Education/training/staff development
  - Occupational health
  - Diagnostic imaging
  - Information technology
- **Adjunct staff members**
  - Infectious diseases
  - Mental health (psychiatry, psychology)
  - Union representatives
  - Human resources
  - Social work
  - Director of house staff/fellowship and other training programs
  - Critical care medicine
  - Pathology
- **State and local health departments**
  - Communicable disease division
  - Laboratory services
  - Medical examiners
- **Community partners**
  - Emergency medical technicians ("first responders")
  - Local law enforcement
  - Funeral service personnel
  - Community service agencies
  - Federally qualified health centers (FQHC)* and other healthcare safety net providers**

*A federally qualified health center (FQHC) is a type of provider defined by the Medicare and Medicaid statutes. FQHCs include health centers receiving grants under section 330 of the Public Health Service Act, certain tribal organizations, and clinics designated by HHS as FQHC Look-Alikes. More information may be found at: http://www.cms.hhs.gov/providers/fqhc/

**Health care safety net providers deliver care to low income and other vulnerable populations, including the uninsured and those covered by Medicaid. Many of these providers have either a legal mandate or an explicit policy to provide services regardless of a patient's ability to pay (http://www.ahcpr.gov/data/safetynet/faq.htm). Major safety net providers include public hospitals and community health centers as well as teaching and community hospitals, and private physicians.

BOX 2. EXAMPLES OF CONSUMABLE AND DURABLE SUPPLY NEEDS

- **Consumable resources**
  - Hand hygiene supplies (antimicrobial soap and alcohol-based, waterless hand hygiene products)
  - Disposable N95, surgical and procedure masks
  - Face shields (disposable or reusable)
  - Gowns
  - Gloves
  - Facial tissues
  - Central line kits
  - Morgue packs
- **Durable resources:**
  - Ventilators
  - Respiratory care equipment
  - Beds
  - IV pumps

TABLE 1. HOSPITAL PANDEMIC INFLUENZA TRIGGERS

Pandemic Influenza Level	Suggested Actions
Interpandemic Period	• Conduct planning • Conduct education/training • Conduct hospital surveillance for influenza (**Supplement 1**)
Pandemic Alert Period	• Increase preparation; refine local plan • Conduct hospital surveillance for influenza (**Supplement 1**)
Pandemic Period • Pandemic influenza outside the United States	• Establish contact with key public health, healthcare, and community partners. • Implement hospital surveillance for pandemic influenza (**Supplement 1**) in incoming patients and previously admitted patients. • Implement a system for early detection and treatment of healthcare personnel who might be infected with the pandemic strain of influenza. • Reinforce infection control procedures to prevent the spread of influenza (**Supplement 4**). • Accelerate staff training in accordance with the facility's pandemic influenza education and training plan.
• Pandemic influenza in the United States	As above, plus: • Implement activities to increase capacity, supplement staff, and provide supplies and equipment. • Maintain close contact with and among healthcare facilities and with state and local health departments. • Post signs for respiratory hygiene/cough etiquette. • Maintain high index of suspicion that patients presenting with influenza-like illness could be infected with pandemic strain. If pandemic strain is detected in local patient, community transmission can be assumed and hospital would move to next level of response.

TABLE 1. HOSPITAL PANDEMIC INFLUENZA TRIGGERS (CONT.)

Pandemic Influenza Level	Suggested Actions

Pandemic Period (cont.)
• Pandemic influenza in the local area
	As above, plus;
	• Emergency department (ED)
	  • Establish segregated waiting areas for persons with symptoms of influenza.
	  • Implement phone triage to discourage unnecessary ED/outpatient department visits.
	  • Enforce respiratory hygiene/cough etiquette.
	• Access controls
	  • Limit number of visitors to those essential for patient support.
	  • Screen all visitors at point of entry to facility for signs and symptoms of influenza.
	  • Limit points of entry to facility; assign clinical staff to entry screening.
	• Hospital admissions
	  • Defer elective admissions and procedures until local epidemic wanes.
	  • Discharge patients as soon as possible.
	  • Cohort patients admitted with influenza.
	  • Monitor for nosocomial transmission.
	• Staffing practices
	  • Consider furlough or reassignment of pregnant staff and other staff at high risk for complications of influenza.
	  • Consider re-assigning non-essential staff to support critical hospital services or placing them on administrative leave; cohort staff caring for influenza patients.
	  • Consider assigning staff recovering from influenza to care for influenza patients.
	  • Implement system for detecting and reporting signs and symptoms of influenza in staff reporting for duty.
	  • Provide staff with antiviral prophylaxis, according to HHS recommendations (See **Supplement 7**).

TABLE 1. HOSPITAL PANDEMIC INFLUENZA TRIGGERS (CONT.)

Pandemic Influenza Level	Suggested Actions

Pandemic Period (cont.)
• Nosocomial transmission
	As above, plus, if nosocomial transmission is limited to only a small number of units in the facility,
	• Close units where there has been nosocomial transmission.
	  • Cohort staff and patients.
	  • Restrict new admissions (except for other pandemic influenza patients) to affected units.
	  • Restrict visitors to the affected units to those who are essential for patient care and support.
	See also **Supplement 4**.

• Widespread transmission in community and hospital; patient admissions at surge capacity	As above plus: • Redirect personnel resources to support patient care (e.g., administrative clinical staff, clinical staff working in departments that have been closed [e.g., physical/occupational therapy, cardiac catheterization]). • Recruit community volunteers (e.g., retired nurses and physicians, clinical staff working in outpatient settings). • Consider placing on administrative leave all non-essential personnel who cannot be reassigned to support critical hospital services.

APPENDIX 1. RESOURCES LIST FOR HEALTHCARE PLANNING

PANDEMIC INFLUENZA PLANS

Currently available State Plans may be found on the following Council of State and Territorial Epidemiologists website: http://www.cste.org/specialprojects/Influenzaplans/StateMap.asp.

Currently available National Plans may be found on the following WHO website: http://www.who.int/csr/disease/influenza/nationalpandemic/en/index.html

WHO Global Influenza Preparedness Plan
(http://www.who.int/csr/resources/publications/influenza/WHO_CDS_CSR_GIP_2005_5/en/index.html)
Document defines the role of WHO and recommendations for national measures before and during pandemics.

WHO Checklist for Influenza Pandemic Preparedness Planning
(http://www.who.int/csr/resources/publications/influenza/WHO_CDS_CSR_GIP_2005_4/en/index.html)

Tools

FluAid
(http://www2.cdc.gov/od/fluaid/default.htm)
FluAid 2.0 provides estimates of the total deaths, hospitalizations, and outpatient visits that might occur during an influenza pandemic.

FluSurge
(http://www.cdc.gov/flu/flusurge.htm)
This specialized spreadsheet-based software estimates the potential surge in demand for hospital-based health care during a pandemic. For each week of a pandemic, FluSurge calculates the potential demand for hospital beds, intensive care unit beds, and mechanical ventilators. Demand for resources is compared with actual capacity. FluSurge is a companion to the previously released FluAid 2.0.

AHRQ's Health Emergency Assistance Line and Triage Hub (HEALTH) Mode
The model is designed to minimize surges in patient demand on the health care delivery system during a bioterrorist event or other public health emergency.

1. Full Report—Health Emergency Assistance Line and Triage Hub (HEALTH) Model (AHRQ Publication No. 05-0040)
   (http://www.ahrq.gov/research/health/health.pdf)
   This report helps planners determine the requirements, specifications, and resources needed for developing an emergency contact center such as the HEALTH model.
2. Contact Center Assessment Tool Set
   (http://www.ahrq.gov/research/health/health.asp)

AHRQ Bioterrorism Planning and Response Resource Page
http://www.ahrq.gov/browse/bioterbr.htm
This resource includes a listing of a variety of tools and resources on issues from community prophylaxis to surge capacity in health facilities.

Emergency Preparedness Resource Inventory (EPRI): A Tool for Local, Regional, and State Planners
(http://www.ahrq.gov/research/epri/)
The Emergency Preparedness Resource Inventory (EPRI) is a tool allowing local or regional planners to assemble an inventory of critical resources that would be useful in responding to a bioterrorist attack. In addition to a Web-based software tool, EPRI includes an Implementation Report, a Technical Manual, and an Appendix.

Altered Standards of Care in Mass Casualty Events
(http://www.ahrq.gov/research/altstand/index.html)
This report discusses the potential of a mass casualty event to compromise the ability of health systems to deliver services meeting established standards of care.

Computer Staffing Model for Bioterrorism Response
(http://www.ahrq.gov/research/biomodel.htm)
This new resource is the Nation's first computerized staffing model that is downloadable as a spreadsheet or accessible as a Web-based version. It can be used to calculate the specific needs of local health care systems based on the number of staff they have and the number of patients they would need to treat quickly in a bioterrorism event.

Rocky Mountain Regional Care Model for Bioterrorist Events: Locate Alternate Care Sites During an Emergency
(http://www.ahrq.gov/research/altsites.htm)
The alternate care site selection tool is designed to allow regional planners to locate and rank potential alternative sites—stadiums, schools, recreation centers, motels, and other venues—based on whether they have adequate ventilation, plumbing, food supply and kitchen facilities, and other factors.

HRSA Bioterrorism and Hospital Preparedness
(http://www.hrsa.gov/bioterrorism/preparationandplanning/healthcare&facilities.htm)
A comprehensive list of resources and documents

ASTHO "Preparedness Planning for State Health Officials – Nature's Terrorist Attack – Pandemic Influenza"
(http://www.astho.org/pubs/PandemicInfluenza.pdf)
Provides checklists for state health officials to assist in preparedness planning. A brief summary of major issues to consider is also included.

Educational Materials samples
(http://www.health.state.ny.us/nysdoh/flu/resources.htm)

HHS healthcare surge capacity document
(http://www.os.hhs.gov/asphep/mscc_handbook.html)

OSHA—Best Practices for the Protection of Hospital-Based First Receivers
(http://www.osha.gov/dts/osta/bestpractices/html/hospital_firstreceivers.html)

ASTM Standard Guide for Hospital Preparedness and Response
The purpose of the guide is to answer questions regarding the minimal levels of preparedness needed for hospitals to deal with a large-scale terrorist attack or other serious emergency and includes guidelines regarding the process for preparedness and mitigation; the process of organizing and planning a hospital response plan; the nature of supplies that hospitals need to make available; the application of existing regulations and guidelines; and an acceptable means to protect the facilities for usual operation, patients, and staff while continuing to provide an effective level of response. (This document is not free to the public, a document summary is available at http://www.astm.org/cgi-bin/SoftCart.exe/DATABASE.CART/REDLINE_PAGES/E2413.htm?L+mystore+vybd9920)

Information on Handling Human Remains During Mass-Casualty Events

- Interim Health Recommendations for Workers who Handle Human Remains
  www.bt.cdc.gov/disasters/tsunamis/handleremains.asp
- Disposing of Liquid Waste from Autopsies in Tsunami-Affected Areas
  www.bt.cdc.gov/disasters/tsunamis/pdf/tsunami-autopsyliquidwaste.pdf

- Management of Dead Bodies in Disaster Situations
  www.paho.org/English/DD/PED/ManejoCadaveres.htm
- Health Concerns Associated with Disaster Victim Identification After a Tsunami—Thailand, Dec 26, 2004–Mar 31, 2005 . MMWR 15 April 2005;54(14):349-52. www.cdc.gov/mmwr/preview/mmwrhtml/mm5414a1.htm

Presentations

2004 AHRQ-sponsored series "Addressing Surge Capacity in a Mass Casualty Event"
(http://www.hsrnet.net/ahrq/surgecapacity/)

Presentations from First National Congress on Public Health Readiness
(http://www.ama-assn.org/ama/noindex/category/11053.html)
(http://www.bt.cdc.gov/training/ncphr/) -CDC Presentations only
These slideshows represent presentations from speakers at the 1st National Congress on Public Health Readiness held July 20-22, 2004.

"No Vacancy: Healthcare Surge Capacity in Disasters."
(http://www.ama-assn.org/ama1/pub/upload/mm/415/hick.ppt)
Jonathan L. Hick, MD, Medical Director, Office of Emergency Preparedness, Hennepin County Medical Center, Minneapolis, Minnesota

Bioterrorism Preparedness: A Hospital Tabletop Exercise
SHEA 14th Annual Scientific Meeting, Philadelphia, PA
April 17, 2004
Prepared by Kelly Henning, MD

APPENDIX 2. HOSPITAL PREPAREDNESS CHECKLIST

Preparedness Subject	Actions Needed
1. Structure for planning and decision making	
❑ An internal, multidisciplinary planning committee for influenza preparedness has been created.	
❑ A person has been designated as the influenza preparedness coordinator. (Insert name) _____	
❑ Members of the planning committee include the following hospital staff members (insert names)	
❑ Administration _____	
❑ Legal counsel _____	
❑ Infection control _____	
❑ Hospital disaster coordinator _____	
❑ Risk management _____	
❑ Facility engineering _____	
❑ Nursing administration _____	
❑ Medical staff _____	
❑ Intensive care _____	
❑ Emergency Department _____	
❑ Laboratory services _____	
❑ Respiratory therapy _____	
❑ Psychiatry _____	
❑ Environmental services _____	
❑ Public relations _____	
❑ Security _____	
❑ Materials management _____	
❑ Staff development _____	
❑ Occupational health _____	
❑ Diagnostic imaging _____	
❑ Pharmacy _____	
❑ Information technology _____	
❑ Other members _____	
❑ Other members _____	

Preparedness Subject	Actions Needed
❑ A state or local health department person has been identified as a committee liaison. (Insert name) _____	
❑ A linkage with local or regional emergency preparedness groups has been established (Planning organization) _____	
2. Development of a written pandemic influenza plan	
❑ A written plan has been completed or is in progress that includes the elements listed in #3 below.	
❑ The plan specifies the circumstances under which the plan will be activated.	
❑ The plan describes the organization structure that will be used to operationalize the plan.	
❑ Responsibilities of key personnel related to executing the plan have been described.	
❑ A simulation exercise has been developed to test the effectiveness of the plan.	
❑ A simulation exercise has been performed. (Date performed _____)	
3. Elements of an influenza pandemic plan	
❑ A **surveillance plan** has been developed. ❑ Syndromic surveillance has been established in the emergency room. ❑ Criteria for distinguishing pandemic influenza is part of the syndromic surveillance plan. ❑ Responsibility has been assigned for reviewing global, national, regional, and local influenza activity trends and informing the pandemic influenza coordinator of evidence of an emerging problem. (Name _____) ❑ Thresholds for heightened local surveillance for pandemic influenza have been established. ❑ A system has been created for internal review of pandemic influenza activity in patients presenting to the emergency department. ❑ A system for monitoring for nosocomial transmission of pandemic has been implemented and tested by monitoring for non-pandemic influenza.	

Preparedness Subject	Actions Needed
❑ A **communication plan** has been developed.	
❑ Responsibility for external communication has been assigned.	
Person responsible for updating public health reporting _____	
Clinical spokesperson for the facility _____	
Media spokesperson for the facility _____	
❑ Key points of contact outside the facility have been identified.	
State health department contact _____	
Local health department contact _____	
Newspaper contact(s) _____	
Radio contact(s) _____	
Public official(s) _____	
❑ A list of other healthcare facilities with whom it will be necessary to maintain communication has been established.	
❑ A meeting with local healthcare facilities has been held to discuss a communication strategy.	
❑ A plan for updating key facility personnel on a daily basis has been established.	
The person(s) responsible for providing these updates are: _____ _____	
❑ A system to track pandemic influenza admissions and discharges has been developed and tested by monitoring non-pandemic influenza admissions and discharges in the community.	
❑ A strategy for regularly updating clinical, ED, and outpatient staff on the status of pandemic influenza, once detected, has been established. (Responsible person _____)	
❑ A plan for informing patients and visitors about the level of pandemic influenza activity has been established.	
❑ An **education and training plan** on pandemic influenza has been developed.	
❑ Language and reading level-appropriate materials for educating all personnel about pandemic influenza and the facility's pandemic influenza plan, have been identified.	
❑ Current and potential sites for long-distance and local education of clinicians on pandemic influenza have been identified.	
❑ Means for accessing state and federal web-based influenza training programs have been identified.	
❑ A system for tracking which personnel have completed pandemic influenza training is in place.	
❑ A plan is in place for rapidly training non-facility staff brought in to provide patient care when the hospital reaches surge capacity. _____	

Preparedness Subject	Actions Needed
❑ The following groups of healthcare personnel have received training on the facility's influenza plan: ❑ Attending physicians ❑ House staff ❑ Nursing staff ❑ Laboratory staff ❑ Emergency Department personnel ❑ Outpatient personnel ❑ Environmental Services personnel ❑ Engineering and maintenance personnel ❑ Security personnel ❑ Nutrition personnel	
❑ A **triage and admission plan** has been developed. ❑ A specific location has been identified for triage of patients with possible pandemic influenza. ❑ The plan includes use of signage to direct and instruct patients with possible pandemic influenza on the triage process. ❑ Patients with possible pandemic influenza will be physically separated from other patients seeking medical attention. ❑ A system for phone triage of patients for purposes of prioritizing patients who require a medical evaluation has been developed. ❑ Criteria for determining which patients need a medical evaluation are in place. ❑ A method for tracking the admission and discharge of patients with pandemic influenza has been developed. ❑ The tracking method has been tested with non-pandemic influenza patients. _____	
❑ A **facility access plan** has been developed. ❑ Criteria and protocols for closing the facility to new admissions are in place. ❑ Criteria and protocols for limiting visitors have been established. ❑ Hospital Security has had input into procedures for enforcing facility access controls. _____	
❑ An **occupational health plan** has been developed. ❑ A system for rapidly delivering vaccine or antiviral prophylaxis to healthcare personnel has been developed. ❑ The system has been tested during a non-pandemic influenza season.	

Preparedness Subject	Actions Needed
❑ A method for prioritizing healthcare personnel for receipt of vaccine or antiviral prophylaxis based on level of patient contact and personal risk for influenza complications has been established. ❑ A system for detecting symptomatic personnel before they report for duty has been developed. ❑ This system has been tested during a non-pandemic influenza period. ❑ A policy for managing healthcare personnel with symptoms of or documented pandemic influenza has been established. The policy considers: ❑ When personnel may return to work after having pandemic influenza ❑ When personnel who are symptomatic but well enough to work, will be permitted to continue working ❑ A method for furloughing or altering the work locations of personnel who are at high risk for influenza complications (e.g., pregnant women, immunocompromised healthcare workers) has been developed. ❑ Mental health and faith-based resources who will provide counseling to personnel during a pandemic have been identified. ❑ A strategy for housing healthcare personnel who may be needed on-site for prolonged periods of time is in place. ❑ A strategy for accommodating and supporting personnel who have child or elder care responsibilities has been developed._____	
❑ A **vaccine and antiviral use** plan has been developed. ❑ A contact for obtaining influenza vaccine has been identified. (Name)_____ ❑ A contact for obtaining antiviral prophylaxis has been identified. (Name)_____ ❑ A priority list (based on HHS guidance for use of vaccines and antivirals in a pandemic when in short supply) and estimated number of patients and healthcare personnel who would be targeted for influenza vaccination or antiviral prophylaxis has been developed. ❑ Number of first priority personnel _____ ❑ Number of second priority personnel _____ ❑ Number of remaining personnel _____ ❑ Number of first priority patients _____ ❑ Number of second priority patients _____ ❑ A system for rapidly distributing vaccine and antivirals to patients has been developed.	

Preparedness Subject	Actions Needed
❑ Issues related to **surge capacity** have been addressed. ❑ A plan is in place to address **unmet staffing needs** in the hospital. ❑ The minimum number and categories of personnel needed to care for a group of patients with pandemic influenza has been determined. ❑ Responsibility for assessing day-to-day clinical staffing needs during an influenza pandemic has been assigned. Persons responsible are: (names and/or titles) _____ _____ ❑ Legal counsel has reviewed emergency laws for using healthcare personnel with out-of-state licenses. ❑ Legal counsel has made sure that any insurance and other liability concerns have been resolved. ❑ Criteria for declaring a "staffing crisis" that would enable the use of emergency staffing alternatives have been defined. ❑ The plan includes linking to local and regional planning and response groups to collaborate on addressing widespread healthcare staffing shortages during a crisis. ❑ A priority list for reassignment and recruitment of personnel has been developed. ❑ A method for rapidly credentialing newly recruited personnel has been developed. ❑ Mutual AID Agreements (MAAs) and Memoranda of Understanding/Agreement (MOU/As) have been signed with other facilities that have agreed to share their staff, as needed. ❑ Strategies to **increase bed capacity** have been identified ❑ A threshold has been established for canceling elective admissions and surgeries ❑ MOAs have been signed with facilities that would accept non-influenza patients in order to free-up bed space ❑ Areas of the facility that could be utilized for expanded bed space have been identified ❑ The estimated patient capacity for this facility is _____ ❑ Plans for expanded bed capacity have been discussed with local and regional planning groups ❑ Anticipated **durable and consumable resource** needs have been determined ❑ A primary plan and contingency plan to address supply shortages has been developed ❑ Plans for obtaining limited resources have been discussed with local and regional planning and response groups.	

Preparedness Subject	Actions Needed
❑ A strategy for handling increased numbers of deceased persons has been developed. ❑ Plans for expanding morgue capacity have been discussed with local and regional planning groups. ❑ Local morticians have been involved in planning discussions. ❑ Mortality estimates have been used to estimate the number of body bags and shrouds. ❑ Supply sources for postmortem materials have been identified. _____	

supplement 4
infection control

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S4-I. RATIONALE

The primary strategies for preventing pandemic influenza are the same as those for seasonal influenza: vaccination, early detection and treatment with antiviral medications (as discussed elsewhere in this plan), and the use of infection control measures to prevent transmission during patient care. However, when a pandemic begins, a vaccine may not yet be widely available, and the supply of antiviral drugs may be limited. The ability to limit transmission in healthcare settings will, therefore, rely heavily on the appropriate and thorough application of infection control measures. While it is commonly accepted that influenza transmission requires close contact—via exposure to large droplets (droplet transmission), direct contact (contact transmission), or near-range exposure to aerosols (airborne transmission)—the relative clinical importance of each of these modes of transmission is not known.

The infection control guidance provided in this supplement is based on our knowledge of routes of influenza transmission (S4-II.A), the pathogenesis of influenza (S4-II.B), and the effects of influenza control measures used during past pandemics and interpandemic periods (S4-II.C) (see also supporting references in the Appendix). Given some uncertainty about the characteristics of a new pandemic strain, all aspects of preparedness planning for pandemic influenza must allow for flexibility and real-time decision-making that take new information into account as the situation unfolds. The specific characteristics of a new pandemic virus—virulence, transmissibility, initial geographic distribution, clinical manifestation, risk to different age groups and subpopulations, and drug susceptibility—will remain unknown until the pandemic gets underway. If the new virus is unusual in any of these respects, HHS and its partners will provide updated infection control guidance.

S4-II. INFLUENZA TRANSMISSION

A. Modes of transmission

Despite the prevalence of influenza year after year, most information on the modes of influenza transmission from person to person is indirect and largely obtained through observations during outbreaks in healthcare facilities and other settings (e.g., cruise ships, airplanes, schools, and colleges); the amount of direct scientific information is very limited. However, the epidemiologic pattern observed is generally consistent with spread through close contact (i.e., exposure to large respiratory droplets, direct contact, or near-range exposure to aerosols). While some observational and animal studies support airborne transmission through small particle aerosols, there is little evidence of airborne transmission over long distances or prolonged periods of time (as is seen with *M. tuberculosis*). The relative contributions and clinical importance of the different modes of influenza transmission are currently unknown.

1. Droplet transmission (www.cdc.gov/ncidod/hip/ISOLAT/std_prec_excerpt.htm)

Droplet transmission involves contact of the conjunctivae or the mucous membranes of the nose or mouth of a susceptible person with large-particle droplets containing microorganisms generated from a person who has a clinical disease or who is a carrier of the microorganism. Droplets are generated from the source person primarily during coughing, sneezing, or talking and during the performance of certain procedures such as suctioning and bronchoscopy. Transmission via large-particle droplets requires close contact between source and recipient persons, because droplets do not remain suspended in the air and generally travel only short distances (about 3 feet) through the air. Because droplets do not remain suspended in the air, special air handling and ventilation are not required to prevent droplet transmission.

Based on epidemiologic patterns of disease transmission, large droplet transmission has been considered a major route of influenza transmission. However, data directly demonstrating large droplet transmission of influenza in human outbreaks is indirect and limited.

2. Contact transmission (www.cdc.gov/ncidod/hip/ISOLAT/contact_prec_excerpt.htm)

Direct-contact transmission involves skin-to-skin contact and physical transfer of microorganisms to a susceptible host from an infected or colonized person, such as occurs when personnel turn patients, bathe patients, or perform other patient-care activities that require physical contact. Direct-contact transmission also can occur between two patients (e.g., by hand contact), with one serving as the source of infectious microorganisms and the other as a susceptible host. Indirect-contact transmission involves contact of a susceptible host with a contaminated intermediate object, usually inanimate, in the patient's environment.

Contact transmission of influenza may occur through either direct skin-to-skin contact or through indirect contact with virus in the environment. Transmission via contaminated hands and fomites has been suggested as a contributing factor in some studies. However, there is insufficient data to determine the proportion of influenza transmission that is attributable to direct or indirect contact.

3. Airborne transmission (www.cdc.gov/ncidod/hip/ISOLAT/airborne_prec_excerpt.htm)

Airborne transmission occurs by dissemination of either airborne droplet nuclei or small particles in the respirable size range containing the infectious agent. Microorganisms carried in this manner—such as *M. tuberculosis*— may be dispersed over long distances by air currents and may be inhaled by susceptible individuals who have not had face-to-face contact with (or been in the same room with) the infectious individual. Organisms transmitted in this manner must be capable of sustaining infectivity, despite desiccation and environmental variation that generally limit survival in the airborne state. Preventing the spread of agents that are transmitted by the airborne route requires the use of special air handling and ventilation systems (e.g., negative pressure rooms).

The relative contribution of airborne transmission to influenza outbreaks is uncertain. Evidence is limited and is principally derived from laboratory studies in animals and some observational studies of influenza outbreaks in humans, particularly on cruise ships and airplanes, where other mechanisms of transmission were also present. Additional information suggesting airborne transmission was reported in a Veterans Administration Hospital study that found lower rates of influenza in wards exposed to ultraviolet radiation (which inactivates influenza viruses) than in wards without UV radiation. Another study indicated that humidity can play a role in the infectivity of aerosolized influenza, although the influence of humidity on the formation of droplet nuclei was not evaluated.

Small-particle aerosols. There is no evidence that influenza transmission can occur across long distances (e.g., through ventilation systems) or through prolonged residence in air, as seen with airborne diseases such as tuberculosis. However, transmission may occur at shorter distances through inhalation of small-particle aerosols (droplet nuclei), particularly in shared air spaces with poor air circulation. An experimental study involving human volunteers found that illness could be induced with substantially lower virus titers when influenza virus was administered as a small droplet aerosol rather than as nasal droplets, suggesting that infection is most efficiently induced when virus is deposited in the lower rather than the upper respiratory tract. While this study supports the possibility of droplet nuclei transmission of influenza, the proportion of infections acquired through droplet nuclei—as compared with large droplet or contact spread—is unknown.

It is likely that some aerosol-generating procedures (e.g., endotracheal intubation, suctioning, nebulizer treatment, bronchosocopy) could increase the potential for dissemination of droplet nuclei in the immediate vicinity of the patient. (Although transmission of SARS-CoV was reported in a Canadian hospital during an aerosol-generating procedure [intubation], it occurred in a situation involving environmental contamination with respiratory secretions.) Although this mode of transmission has not been evaluated for influenza, additional precautions for healthcare personnel who perform aerosol-generating procedures on influenza patients may be warranted.

B. Pathogenesis of influenza and implications for infection control

The cellular pathogenesis of human influenza indicates that infection principally takes place within the respiratory tract. While conjunctivitis is a common manifestation of systemic influenza infection, the ocular route of inoculation and infection has not been demonstrated for human influenza viruses. This may not be true with certain avian species of influenza (e.g., H7N7) that have been associated primarily with conjunctivitis in humans.[1] This information suggests that preventing direct and indirect inoculation of the respiratory tract is of utmost importance for preventing person-to-person transmission when caring for infectious patients.

C. Control of transmission in healthcare facilities

Outbreaks of influenza have been prevented or controlled through a set of well established strategies that include vaccination of patients and healthcare personnel; early detection of influenza cases in a facility; use of antivirals to treat ill persons and, if recommended, as prophylaxis; isolation of infectious patients in private rooms or cohort units; use of appropriate barrier precautions during patient care, as recommended for Standard and Droplet Precautions (Box 1); and administrative measures, such as restricting visitors, educating patients and staff, and cohorting healthcare workers assigned to an outbreak unit.

These are the primary infection control measures recommended in this plan. They will be updated, as necessary, based on the observed characteristics of the pandemic influenza virus.

S4-III. OVERVIEW

Supplement 4 provides guidance to healthcare and public health partners on basic principles of infection control for limiting the spread of pandemic influenza. These principles (summarized in Box 1) are common to the prevention of other infectious agents spread by respiratory droplets. **Supplement 4** also includes guidance on the selection and use of personal protective equipment (PPE); hand hygiene and safe work practices; cleaning and disinfection of environmental surfaces; handling of laboratory specimens; and post-mortem care. The guidance also covers infection control practices related to the management of infectious patients, the protection of persons at high-risk for severe influenza or its complications, and issues concerning occupational health.

Supplement 4 also provides guidance on how to adapt infection control practices in specific healthcare settings, including hospitals, nursing homes and other long-term care facilities, pre-hospital care (emergency medical services [EMS]), medical offices and other ambulatory care settings, and during the provision of professional home healthcare services. The section on hospital care covers detection of entering patients who may be infected with pandemic influenza; implementation of source-control measures to limit virus dissemination from respiratory secretions; hospitalization of pandemic influenza patients; and detection and control of nosocomial transmission.

In addition, **Supplement 4** includes guidance on infection control procedures for pandemic influenza patients in the home or in alternative care sites that may be established if local hospital capacity is overwhelmed by a pandemic. Finally, it includes recommendations on infection control in schools, workplaces, and community settings.

Supplement 4 does not address the use of vaccines and antivirals in the control of influenza transmission in healthcare settings and the community. These issues are addressed in **Supplements 6 and 7**, respectively.

[1] Eye protection is recommended when working with conjunctivitis-inducing avian influenza viruses

S4-IV. RECOMMENDATIONS FOR INFECTION CONTROL IN HEALTHCARE SETTINGS

The recommendations for infection control described below are generally applicable throughout the different pandemic phases. In some cases, as indicated, recommendations may be modified as the situation progresses from limited cases to widespread community illness.

A. Basic infection control principles for preventing the spread of pandemic influenza in healthcare settings

The following infection control principles apply in any setting where persons with pandemic influenza might seek and receive healthcare services (e.g. hospitals, emergency departments, out-patient facilities, residential care facilities, homes). Details of how these principles may be applied in each healthcare setting follow.

- Limit contact between infected and non-infected persons[2]
  - Isolate infected persons (i.e., confine patients to a defined area as appropriate for the healthcare setting).
  - Limit contact between nonessential personnel and other persons (e.g., social visitors) and patients who are ill with pandemic influenza.
  - Promote spatial separation in common areas (i.e., sit or stand as far away as possible—at least 3 feet—from potentially infectious persons) to limit contact between symptomatic and non-symptomatic persons.
- Protect persons caring for influenza patients in healthcare settings from contact with the pandemic influenza virus. Persons who must be in contact should:
  - Wear a surgical or procedure mask[3] for close contact with infectious patients.
  - Use contact and airborne precautions, including the use of N95 respirators, when appropriate [S4-IV.C].
  - Wear gloves (gown if necessary) for contact with respiratory secretions.
  - Perform hand hygiene after contact with infectious patients.
- Contain infectious respiratory secretions:
  - Instruct persons who have "flu-like" symptoms (see below) to use respiratory hygiene/cough etiquette (See Box 2).
  - Promote use of masks[4] by symptomatic persons in common areas (e.g., waiting rooms in physician offices or emergency departments) or when being transported (e.g., in emergency vehicles).

Symptoms of influenza include fever, headache, myalgia, prostration, coryza, sore throat, and cough. Otitis media, nausea, and vomiting are also commonly reported among children. Typical influenza (or "flu-like") symptoms, such as fever, may not always be present in elderly patients, young children, patients in long-term care facilities, or persons with underlying chronic illnesses (see **Supplement** 5, Box 2).

[2] During the early stages of a pandemic, laboratory-confirmation of influenza infection is recommended when possible.

[3] Surgical masks come in two basic types: one type is affixed to the head with two ties, conforms to the face with the aid of a flexible adjustment for the nose bridge, and may be flat/pleated or duck-billed in shape; the second type of surgical mask is pre-molded, adheres to the head with a single elastic and has a flexible adjustment for the nose bridge. Procedure masks are flat/pleated and affix to the head with ear loops. All masks have some degree of fluid resistance but those approved as surgical masks must meet specified standards for protection from penetration of blood and body fluids.

[4] Coughing persons may wear either a surgical or procedure mask. However, only procedure masks come in both adult and pediatric sizes.

B. Management of infectious patients

1. Respiratory hygiene/cough etiquette

Respiratory hygiene/cough etiquette has been promoted as a strategy to contain respiratory viruses at the source and to limit their spread in areas where infectious patients might be awaiting medical care (e.g., physician offices, emergency departments) (see S4-IV.B.2).

The impact of covering sneezes and coughs and/or placing a mask on a coughing patient on the containment of respiratory secretions or on the transmission of respiratory infections has not been systematically studied. In theory, however, any measure that limits the dispersal of respiratory droplets should reduce the opportunity for transmission. Masking may be difficult in some settings, e.g., pediatrics, in which case the emphasis will be on cough hygiene.

The elements of respiratory hygiene/cough etiquette include:

- Education of healthcare facility staff, patients, and visitors on the importance of containing respiratory secretions to help prevent the transmission of influenza and other respiratory viruses
- Posted signs in languages appropriate to the populations served with instructions to patients and accompanying family members or friends to immediately report symptoms of a respiratory infection as directed
- Source control measures (e.g., covering the mouth/nose with a tissue when coughing and disposing of used tissues; using masks on the coughing person when they can be tolerated and are appropriate)
- Hand hygiene after contact with respiratory secretions, and
- Spatial separation, ideally >3 feet, of persons with respiratory infections in common waiting areas when possible.

2. Droplet precautions and patient placement

Patients with known or suspected pandemic influenza should be placed on droplet precautions for a minimum of 5 days from the onset of symptoms. Because immunocompromised patients may shed virus for longer periods, they may be placed on droplet precautions for the duration of their illness. Healthcare personnel should wear appropriate PPE (see S4-IV.C). The placement of patients will vary depending on the healthcare setting (see setting-specific guidance).

If the pandemic virus is associated with diarrhea, contact precautions (i.e., gowns and gloves for all patient contact) should be added.

CDC will update these recommendations if changes occur in the anticipated pattern of transmission (www.cdc.gov/flu).

C. Infection control practices for healthcare personnel

Infection control practices for pandemic influenza are the same as for other human influenza viruses and primarily involve the application of standard and droplet precautions (Box 1) during patient care in healthcare settings (e.g., hospitals, nursing homes, outpatient offices, emergency transport vehicles). This guidance also applies to healthcare personnel going into the homes of patients. During a pandemic, conditions that could affect infection control may include shortages of antiviral drugs, decreased efficacy of the vaccine, increased virulence of the influenza strain, shortages of single-patient rooms, and shortages of personal protective equipment. These issues may necessitate changes in the standard recommended infection control practices for influenza. CDC will provide updated infection control guidance as circumstances dictate. Additional guidance is provided for family members providing home care (S4-IV.G) and for use in public settings (e.g., schools, workplace) where people with pandemic influenza may be encountered (S4-V and S4-VI).

1. Personal protective equipment

a) PPE for standard and droplet precautions

PPE is used to prevent direct contact with the pandemic influenza virus. PPE that may be used to provide care includes surgical or procedure masks, as recommended for droplet precautions, and gloves and gowns, as recommended for standard precautions (Box 1). Additional precautions may be indicated during the performance of aerosol-generating procedures (see below). Information on the selection and use of PPE is provided at www.cdc.gov/ncidod/hip/isolat/isolat.htm/.

- **Masks (surgical or procedure)**
  - Wear a mask when entering a patient's room. A mask should be worn once and then discarded. If pandemic influenza patients are cohorted in a common area or in several rooms on a nursing unit, and multiple patients must be visited over a short time, it may be practical to wear one mask for the duration of the activity; however, other PPE (e.g., gloves, gown) must be removed between patients and hand hygiene performed.
  - Change masks when they become moist.
  - Do not leave masks dangling around the neck.
  - Upon touching or discarding a used mask, perform hand hygiene.
- **Gloves**
  - A single pair of patient care gloves should be worn for contact with blood and body fluids, including during hand contact with respiratory secretions (e.g., providing oral care, handling soiled tissues). Gloves made of latex, vinyl, nitrile, or other synthetic materials are appropriate for this purpose; if possible, latex-free gloves should be available for healthcare workers who have latex allergy.
  - Gloves should fit comfortably on the wearer's hands.
  - Remove and dispose of gloves after use on a patient; do not wash gloves for subsequent reuse.
  - Perform hand hygiene after glove removal.
  - If gloves are in short supply (i.e., the demand during a pandemic could exceed the supply), priorities for glove use might need to be established. In this circumstance, reserve gloves for situations where there is a likelihood of extensive patient or environmental contact with blood or body fluids, including during suctioning.
  - Use other barriers (e.g., disposable paper towels, paper napkins) when there is only limited contact with a patient's respiratory secretions (e.g., to handle used tissues). Hand hygiene should be strongly reinforced in this situation.
- **Gowns**
  - Wear an isolation gown, if soiling of personal clothes or uniform with a patient's blood or body fluids, including respiratory secretions, is anticipated. **Most patient interactions do not necessitate the use of gowns.** However, procedures such as intubation and activities that involve holding the patient close (e.g., in pediatric settings) are examples of when a gown may be needed when caring for pandemic influenza patients.
  - A disposable gown made of synthetic fiber or a washable cloth gown may be used.
  - Ensure that gowns are of the appropriate size to fully cover the area to be protected.
  - Gowns should be worn only once and then placed in a waste or laundry receptacle, as appropriate, and hand hygiene performed.
  - If gowns are in short supply (i.e., the demand during a pandemic could exceed the supply) priorities for their use may need to be established. In this circumstance, reinforcing the situations in which they are needed can reduce the volume used. Alternatively, other coverings (e.g., patient gowns) could be used. It is doubtful that disposable aprons would provide the desired protection in the circumstances where gowns are needed to prevent contact with

influenza virus, and therefore should be avoided. There are no data upon which to base a recommendation for reusing an isolation gown on the same patient. To avoid possible contamination, it is prudent to limit this practice.

- **Goggles or face shield**

  In general, wearing goggles or a face shield for routine contact with patients with pandemic influenza is not necessary. If sprays or splatter of infectious material is likely, goggles or a face shield should be worn as recommended for standard precautions. Additional information related to the use of eye protection for infection control can be found at http://www.cdc.gov/niosh/topics/eye/eye-infectious.html.

b) PPE for special circumstances

- **PPE for aerosol-generating procedures**

  During procedures that may generate increased small-particle aerosols of respiratory secretions (e.g., endotracheal intubation, nebulizer treatment, bronchoscopy, suctioning), healthcare personnel should wear gloves, gown, face/eye protection, and a N95 respirator or other appropriate particulate respirator. Respirators should be used within the context of a respiratory protection program that includes fit-testing, medical clearance, and training. If possible, and when practical, use of an airborne isolation room may be considered when conducting aerosol-generating procedures.

- **PPE for managing pandemic influenza with increased transmissibility**

  The addition of airborne precautions, including respiratory protection (an N95 filtering face piece respirator or other appropriate particulate respirator), may be considered for strains of influenza exhibiting increased transmissibility, during initial stages of an outbreak of an emerging or novel strain of influenza, and as determined by other factors such as vaccination/immune status of personnel and availability of antivirals. As the epidemiologic characteristics of the pandemic virus are more clearly defined, CDC will provide updated infection control guidance, as needed.

- **Precautions for early stages of a pandemic**

  Early in a pandemic, it may not be clear that a patient with severe respiratory illness has pandemic influenza. Therefore precautions consistent with all possible etiologies, including a newly emerging infectious agent, should be implemented. This may involve the combined use of airborne and contact precautions, in addition to standard precautions, until a diagnosis is established.

c) Caring for patients with pandemic influenza

Healthcare personnel should be particularly vigilant to avoid:

- Touching their eyes, nose or mouth with contaminated hands (gloved or ungloved). Careful placement of PPE before patient contact will help avoid the need to make PPE adjustments and risk self-contamination during use. Careful removal of PPE is also important. (See also: http://www.cdc.gov/ncidod/hip/ppe/default.htm.)
- Contaminating environmental surfaces that are not directly related to patient care (e.g., door knobs, light switches)

2. Hand hygiene

Hand hygiene has frequently been cited as the single most important practice to reduce the transmission of infectious agents in healthcare settings (see http://www.cdc.gov/handhygiene/pressrelease.htm) and is an essential element of standard precautions. The term "hand hygiene" includes both handwashing with either plain or antimicrobial soap and water and use of alcohol-based products (gels, rinses, foams) containing an emollient that do not require the use of water.

- If hands are visibly soiled or contaminated with respiratory secretions, wash hands with soap (either non-antimicrobial or antimicrobial) and water.

- In the absence of visible soiling of hands, approved alcohol-based products for hand disinfection are preferred over antimicrobial or plain soap and water because of their superior microbiocidal activity, reduced drying of the skin, and convenience.
- Always perform hand hygiene between patient contacts and after removing PPE.
- Ensure that resources to facilitate handwashing (i.e., sinks with warm and cold running water, plain or antimicrobial soap, disposable paper towels) and hand disinfection (i.e., alcohol-based products) are readily accessible in areas in which patient care is provided. For additional guidance on hand hygiene see http://www.cdc.gov/handhygiene/.

3. Disposal of solid waste

Standard precautions are recommended for disposal of solid waste (medical and non-medical) that might be contaminated with a pandemic influenza virus:

- Contain and dispose of contaminated medical waste in accordance with facility-specific procedures and/or local or state regulations for handling and disposal of medical waste, including used needles and other sharps, and non-medical waste.
- Discard as routine waste used patient-care supplies that are not likely to be contaminated (e.g., paper wrappers).
- Wear disposable gloves when handling waste. Perform hand hygiene after removal of gloves.

4. Linen and laundry

Standard precautions are recommended for linen and laundry that might be contaminated with respiratory secretions from patients with pandemic influenza:

- Place soiled linen directly into a laundry bag in the patient's room. Contain linen in a manner that prevents the linen bag from opening or bursting during transport and while in the soiled linen holding area.
- Wear gloves and gown when directly handling soiled linen and laundry (e.g., bedding, towels, personal clothing) as per standard precautions. Do not shake or otherwise handle soiled linen and laundry in a manner that might create an opportunity for disease transmission or contamination of the environment.
- Wear gloves for transporting bagged linen and laundry.
- Perform hand hygiene after removing gloves that have been in contact with soiled linen and laundry.
- Wash and dry linen according to routine standards and procedures (www.cdc.gov/ncidod/hip/enviro/guide.htm).

5. Dishes and eating utensils

Standard precautions are recommended for handling dishes and eating utensils used by a patient with known or possible pandemic influenza:

- Wash reusable dishes and utensils in a dishwasher with recommended water temperature (www.cdc.gov/ncidod/hip/enviro/guide.htm).
- Disposable dishes and utensils (e.g., used in an alternative care site set-up for large numbers of patients) should be discarded with other general waste.
- Wear gloves when handling patient trays, dishes, and utensils.

6. Patient-care equipment

Follow standard practices for handling and reprocessing used patient-care equipment, including medical devices:

- Wear gloves when handling and transporting used patient-care equipment.

- Wipe heavily soiled equipment with an EPA-approved hospital disinfectant before removing it from the patient's room. Follow current recommendations for cleaning and disinfection or sterilization of reusable patient-care equipment.
- Wipe external surfaces of portable equipment for performing x-rays and other procedures in the patient's room with an EPA-approved hospital disinfectant upon removal from the patient's room.

7. Environmental cleaning and disinfection

Cleaning and disinfection of environmental surfaces are important components of routine infection control in healthcare facilities. Environmental cleaning and disinfection for pandemic influenza follow the same general principles used in healthcare settings.

a) Cleaning and disinfection of patient-occupied rooms
(See: www.cdc.gov/ncidod/hip/enviro/Enviro_guide_03.pdf)

- Wear gloves in accordance with facility policies for environmental cleaning and wear a surgical or procedure mask in accordance with droplet precautions. Gowns are not necessary for routine cleaning of an influenza patient's room.
- Keep areas around the patient free of unnecessary supplies and equipment to facilitate daily cleaning.
- Use any EPA-registered hospital detergent-disinfectant. Follow manufacturer's recommendations for use-dilution (i.e., concentration), contact time, and care in handling.
- Follow facility procedures for regular cleaning of patient-occupied rooms. Give special attention to frequently touched surfaces (e.g., bedrails, bedside and over-bed tables, TV controls, call buttons, telephones, lavatory surfaces including safety/pull-up bars, doorknobs, commodes, ventilator surfaces) in addition to floors and other horizontal surfaces.
- Clean and disinfect spills of blood and body fluids in accordance with current recommendations for Isolation Precautions (www.cdc.gov/ncidod/hip/ISOLAT/Isolat.htm).

b) Cleaning and disinfection after patient discharge or transfer

- Follow standard facility procedures for post-discharge cleaning of an isolation room.
- Clean and disinfect all surfaces that were in contact with the patient or might have become contaminated during patient care. No special treatment is necessary for window curtains, ceilings, and walls unless there is evidence of visible soiling.
- Do not spray (i.e., fog) occupied or unoccupied rooms with disinfectant. This is a potentially dangerous practice that has no proven disease control benefit.

8. Postmortem care

Follow standard facility practices for care of the deceased. Practices should include standard precautions for contact with blood and body fluids.

9. Laboratory specimens and practices

Follow standard facility and laboratory practices for the collection, handling, and processing of laboratory specimens.

D. Occupational health issues

Healthcare personnel are at risk for pandemic influenza through community and healthcare-related exposures. Once pandemic influenza has reached a community, healthcare facilities must implement systems to monitor for illness in the facility workforce and manage those who are symptomatic or ill.

- Implement a system to educate personnel about occupational health issues related to pandemic influenza.
- Screen all personnel for influenza-like symptoms before they come on duty. Symptomatic personnel should be sent home until they are physically ready to return to duty.
- Healthcare personnel who have recovered from pandemic influenza, and should develop antibody against future infection with the same virus, and therefore should be prioritized for the care of patients with active pandemic influenza and its complications. These workers would also be well suited to care for patients who are at risk for serious complications from influenza (e.g., transplant patients and neonates).
- Personnel who are at high risk for complications of pandemic influenza (e.g., pregnant women, immunocompromised persons) should be informed about their medical risk and offered an alternate work assignment, away from influenza-patient care, or considered for administrative leave until pandemic influenza has abated in the community.

E. Reducing exposure of persons at high risk for complications of influenza

Persons who are well, but at high risk for influenza or its complications (e.g., persons with underlying diseases), should be instructed to avoid unnecessary contact with healthcare facilities caring for pandemic influenza patients (i.e., do not visit patients, postpone nonessential medical care).

F. Healthcare setting-specific guidance

All healthcare facilities should follow the infection control guidance in S4-IV.A-E above. The following guidance is intended to address setting-specific infection control issues that should also be considered.

1. Hospitals

a) Detection of persons entering the facility who may have pandemic influenza

- Post visual alerts (in appropriate languages) at the entrance to hospital outpatient facilities (e.g., emergency departments, outpatient clinics) instructing persons with respiratory symptoms (e.g., patients, persons who accompany them) to:
  - Inform reception and healthcare personnel when they first register for care, and
  - Practice respiratory hygiene/cough etiquette (see www.cdc.gov/flu/professionals/infectioncontrol/resphygiene.htm).

  Sample visual alerts are available on CDC's SARS website: http://www.cdc.gov/ncidod/hip/INFECT/RespiratoryPoster.pdf
- Triage patients calling for medical appointments for influenza symptoms:
  - Discourage unnecessary visits to medical facilities.
  - Instruct symptomatic patients on infection control measures to limit transmission in the home and when traveling to necessary medical appointments.

As the scope of the pandemic escalates locally, consider setting up a separate triage area for persons presenting with symptoms of respiratory infection. Because not every patient presenting with symptoms will have pandemic influenza, infection control measures will be important in preventing further spread.

- During the peak of a pandemic, emergency departments and outpatient offices may be overwhelmed with patients seeking care. A "triage officer" may be useful for managing patient flow, including deferral of patients who do not require emergency care.
- Designate separate waiting areas for patients with influenza-like symptoms. If this is not feasible, the waiting area should be set up to enable patients with respiratory symptoms to sit as far away as possible (at least 3 feet) from other patients.

b) "Source control" measures to limit dissemination of influenza virus from respiratory secretions

- Post signs that promote respiratory hygiene/cough etiquette in common areas (e.g., elevators, waiting areas, cafeterias, lavatories) where they can serve as reminders to all persons in the healthcare facility. Signs should instruct persons to:
  - Cover the nose/mouth when coughing or sneezing.
  - Use tissues to contain respiratory secretions.
  - Dispose of tissues in the nearest waste receptacle after use.
  - Perform hand hygiene after contact with respiratory secretions.
    Samples of visual alerts are available on CDC's SARS website: http://www.cdc.gov/ncidod/hip/INFECT/RespiratoryPoster.pdf
- Facilitate adherence to respiratory hygiene/cough etiquette by ensuring the availability of materials in waiting areas for patients and visitors.
  - Provide tissues and no-touch receptacles (e.g., waste containers with pedal-operated lid or uncovered waste container) for used tissue disposal.
  - Provide conveniently located dispensers of alcohol-based hand rub.
  - Provide soap and disposable towels for handwashing where sinks are available.
- Promote the use of masks and spatial separation by persons with symptoms of influenza.
  - Offer and encourage the use of either procedure masks (i.e., with ear loops) or surgical masks (i.e., with ties or elastic) by symptomatic persons to limit dispersal of respiratory droplets.
  - Encourage coughing persons to sit as far away as possible (at least 3 feet) from other persons in common waiting areas.

c) Hospitalization of pandemic influenza patients

- Patient placement
  - Limit admission of influenza patients to those with severe complications of influenza who cannot be cared for outside the hospital setting.
  - Admit patients to either a single-patient room or an area designated for cohorting of patients with influenza.
- Cohorting
  - Designated units or areas of a facility should be used for cohorting patients with pandemic influenza.[6] During a pandemic, other respiratory viruses (e.g., non-pandemic influenza, respiratory syncytial virus, parainfluenza virus) may be circulating concurrently in a community. Therefore, to prevent cross-transmission of respiratory viruses, whenever possible assign only patients with confirmed pandemic influenza to the same room. At the height of a pandemic, laboratory testing to confirm pandemic influenza is likely to be limited, in which case cohorting should be based on having symptoms consistent with pandemic influenza.
  - Personnel (clinical and non-clinical) assigned to cohorted patient care units for pandemic influenza patients should not "float" or otherwise be assigned to other patient care areas. The number of personnel entering the cohorted area should be limited to those necessary for patient care and support.
  - Personnel assigned to cohorted patient care units should be aware that patients with pandemic influenza may be concurrently infected or colonized with other pathogenic organisms (e.g., *Staphylococcus aureus, Clostridium*

[6] During the early stages of a pandemic, laboratory-confirmation of influenza infection is recommended when possible before cohorting patients.

difficile) and should adhere to infection control practices (e.g., hand hygiene, changing gloves between patient contact) used routinely, and as part of standard precautions, to prevent nosocomial transmission.

- Because of the high patient volume anticipated during a pandemic, cohorting should be implemented early in the course of a local outbreak.

- Patient transport
  - Limit patient movement and transport outside the isolation area to medically necessary purposes.
  - Consider having portable x-ray equipment available in areas designated for cohorting influenza patients.
  - If transport or movement is necessary, ensure that the patient wears a surgical or procedure mask. If a mask cannot be tolerated (e.g., due to the patient's age or deteriorating respiratory status), apply the most practical measures to contain respiratory secretions. Patients should perform hand hygiene before leaving the room.

- Visitors
  - Screen visitors for signs and symptoms of influenza before entry into the facility and exclude persons who are symptomatic.
  - Family members who accompany patients with influenza-like illness to the hospital are assumed to have been exposed to influenza and should wear masks.
  - Limit visitors to persons who are necessary for the patient's emotional well-being and care.
  - Instruct visitors to wear surgical or procedure masks while in the patient's room.
  - Instruct visitors on hand-hygiene practices.

d) Control of nosocomial pandemic influenza transmission

- Once patients with pandemic influenza are admitted to the hospital, nosocomial surveillance should be heightened for evidence of transmission to other patients and healthcare personnel. (Once pandemic influenza is firmly established in a community this may not be feasible or necessary.)
- If limited nosocomial transmission is detected (e.g., has occurred on one or two patient care units), appropriate control measures should be implemented. These may include:
  - Cohorting of patients and staff on affected units
  - Restriction of new admissions (except for other pandemic influenza patients) to the affected unit(s)
  - Restriction of visitors to the affected unit(s) to those who are essential for patient care and support
- If widespread nosocomial transmission occurs, controls may need to be implemented hospital wide and might include:
  - Restricting all nonessential persons
  - Stopping admissions not related to pandemic influenza and stopping elective surgeries

2. Nursing homes and other residential facilities

Residents of nursing homes and other residential facilities will be at particular risk for transmission of pandemic influenza and disease complications. Pandemic influenza can be introduced through facility personnel and visitors; once a pandemic influenza virus enters such facilities, controlling its spread is problematic. Therefore, as soon as pandemic influenza has been detected in the region, nursing homes and other residential facilities should implement aggressive measures to prevent introduction of the virus.

a) Prevention or delay of pandemic influenza virus entry into the facility

- Control of visitors
  - Post visual alerts (in appropriate languages) at the entrance to the facility restricting entry by persons who have been exposed to or have symptoms of pandemic influenza.
  - Enforce visitor restrictions by assigning personnel to verbally and visually screen visitors for respiratory symptoms at points of entry to the facility.
  - Provide a telephone number where persons can call for information on measures used to prevent the introduction of pandemic influenza.
- Control of personnel
  - Implement a system to screen all personnel for influenza-like symptoms before they come on duty. Symptomatic personnel should be sent home until they are physically able to return to duty.

b) Monitoring patients for pandemic influenza and instituting appropriate control measures

Despite aggressive efforts to prevent the introduction of pandemic influenza virus, persons in the early stages of pandemic influenza could introduce it to the facility. Residents returning from a hospital stay, outpatient visit, or family visit could also introduce the virus. Early detection of the presence of pandemic influenza in a facility is critical for ensuring timely implementation of infection control measures.

- Early in the progress of a pandemic in the region, increase resident surveillance for influenza-like symptoms. Notify state or local health department officials if a case(s) is suspected.
- If symptoms of pandemic influenza are apparent (see **Supplement 5)**, implement droplet precautions for the resident and roommates, pending confirmation of pandemic influenza virus infection. Patients and roommates should not be separated or moved out of their rooms unless medically necessary. Once a patient has been diagnosed with pandemic influenza, roommates should be treated as exposed cohorts.
- Cohort residents and staff *on units with known or suspected cases of pandemic influenza*.
- Limit movement within the facility (e.g., temporarily close the dining room and serve meals on nursing units, cancel social and recreational activities).

3. Prehospital care (emergency medical services)

Patients with severe pandemic influenza or disease complications are likely to require emergency transport to the hospital. The following information is designed to protect EMS personnel during transport.

- Screen patients requiring emergency transport for symptoms of influenza.
- Follow standard and droplet precautions when transporting symptomatic patients.
- Consider routine use of surgical or procedure masks for all patient transport when pandemic influenza is in the community.
- If possible, place a procedure or surgical mask on the patient to contain droplets expelled during coughing. If this is not possible (i.e., would further compromise respiratory status, difficult for the patient to wear), have the patient cover the mouth/nose with tissue when coughing, or use the most practical alternative to contain respiratory secretions.
- Oxygen delivery with a non-rebreather face mask can be used to provide oxygen support during transport. If needed, positive-pressure ventilation should be performed using a resuscitation bag-valve mask.
- Unless medically necessary to support life, aerosol-generating procedures (e.g., mechanical ventilation) should be avoided during prehospital care.

- Optimize the vehicle's ventilation to increase the volume of air exchange during transport. When possible, use vehicles that have separate driver and patient compartments that can provide separate ventilation to each area.
- Notify the receiving facility that a patient with possible pandemic influenza is being transported.
- Follow standard operating procedures for routine cleaning of the emergency vehicle and reusable patient care equipment.

4. Home healthcare services

Home healthcare includes health and rehabilitative services performed in the home by providers including home health agencies, hospices, durable medical equipment providers, home infusion therapy services, and personal care and support services staff. The scope of services ranges from assistance with activities of daily living and physical and occupational therapy to wound care, infusion therapy, and chronic ambulatory peritoneal dialysis (CAPD). Communication between home healthcare providers and patients or their family members is essential for ensuring that these personnel are appropriately protected.

When pandemic influenza is in the community, home health agencies should consider contacting patients before the home visit to determine whether persons in the household have an influenza-like illness.

- If patients with pandemic influenza are in the home, consider:
  - Postponing nonessential services
  - Assigning providers who are not at increased risk for complications of pandemic influenza to care for these patients
- Home healthcare providers who enter homes where there is a person with an influenza-like illness should follow the recommendations for standard and droplet precautions described above. Professional judgment should be used in determining whether to don a surgical or procedure mask upon entry into the home or only for patient interactions. Factors to consider include the possibility that others in the household may be infectious and the extent to which the patient is ambulating within the home.

5. Outpatient medical offices

Patients with nonemergency symptoms of an influenza-like illness may seek care from their medical provider. Implementation of infection control measures when these patients present for care will help prevent exposure among other patients and clinical and nonclinical office staff.

a) Detection of patients with possible pandemic influenza

- Post visual alerts (in appropriate languages) at the entrance to outpatient offices instructing persons with respiratory symptoms (e.g., patients, persons who accompany them) to:
  - Inform reception and healthcare personnel when they first register for care
  - Practice respiratory hygiene/cough etiquette (see www.cdc.gov/flu/professionals/infectioncontrol/resphygiene.htm)

  Sample visual alerts may be found on CDC's SARS website: http://www.cdc.gov/ncidod/hip/INFECT/RespiratoryPoster.pdf
- Triage patients calling for medical appointments for influenza symptoms:
  - Discourage unnecessary visits to medical facilities.
  - Instruct symptomatic patients on infection control measures to limit transmission in the home and when traveling to necessary medical appointments.

b) "Source control" measures

- Post signs that promote cough etiquette in common areas (e.g., elevators, waiting areas, cafeterias, lavatories) where they can serve as reminders to all persons in the healthcare facility. Signs should instruct persons to:

- Cover the nose/mouth when coughing or sneezing.
- Use tissues to contain respiratory secretions.
- Dispose of tissues in the nearest waste receptacle after use.
- Perform hand hygiene after contact with respiratory secretions.

- Facilitate adherence to respiratory hygiene/cough etiquette. Ensure the availability of materials in waiting areas for patients and visitors.
  - Provide tissues and no-touch receptacles (e.g., waste containers with pedal-operated lid or uncovered waste container) for used tissue disposal.
  - Provide conveniently located dispensers of alcohol-based hand rub.
  - Provide soap and disposable towels for hand washing where sinks are available.
- Promote the use of procedure or surgical masks and spatial separation by persons with symptoms of influenza.
  - Offer and encourage the use of either procedure masks (i.e., with ear loops) or surgical masks (i.e., with ties or elastic) by symptomatic persons to limit dispersal of respiratory droplets.
  - Encourage coughing persons to sit at least 3 feet away from other persons in common waiting areas.

c) Patient placement

- Where possible, designate separate waiting areas for patients with symptoms of pandemic influenza. Place signs indicating the separate waiting areas.
- Place symptomatic patients in an evaluation room as soon as possible to limit their time in common waiting areas.

6. Other ambulatory settings

A wide variety of ambulatory settings provide chronic (e.g., hemodialysis units) and episodic (e.g., freestanding surgery centers, dental offices) healthcare services. When pandemic influenza is in the region, these facilities should implement control measures similar to those recommended for outpatient physician offices. Other infection control strategies that may be utilized include:

- Screening patients for influenza-like illness by phone or before coming into the facility and rescheduling appointments for those whose care is nonemergency
- Canceling all nonemergency services when there is pandemic influenza in the community

G. Care of pandemic influenza patients in the home

Most patients with pandemic influenza will be able to remain at home during the course of their illness and can be cared for by other family members or others who live in the household. Anyone residing in a household with an influenza patient during the incubation period and illness is at risk for developing influenza. A key objective in this setting is to limit transmission of pandemic influenza within and outside the home. When care is provided by a household member, basic infection control precautions should be emphasized (e.g., segregating the ill patient, hand hygiene). Infection within the household may be minimized if a primary caregiver is designated, ideally someone who does not have an underlying condition that places them at increased risk of severe influenza disease. Although no studies have assessed the use of masks at home to decrease the spread of infection, use of surgical or procedure masks by the patient and/or caregiver during interactions may be of benefit.

1. Management of influenza patients

- Physically separate the patient with influenza from non-ill persons living in the home as much as possible.
- Patients should not leave the home during the period when they are most likely to be infectious to others (i.e., 5 days after onset of symptoms). When movement outside the home is necessary (e.g., for medical care), the patient should

follow cough etiquette (i.e., cover the mouth and nose when coughing and sneezing) and wear procedure or surgical masks if available.

2. Management of other persons in the home

- Persons who have not been exposed to pandemic influenza and who are not essential for patient care or support should not enter the home while persons are actively ill with pandemic influenza.
- If unexposed persons must enter the home, they should avoid close contact with the patient.
- Persons living in the home with the pandemic influenza patient should limit contact with the patient to the extent possible; consider designating one person as the primary care provider.
- Household members should monitor closely for the development of influenza symptoms and contact a telephone hotline or medical care provider if symptoms occur.

3. Infection control measures in the home

- All persons in the household should carefully follow recommendations for hand hygiene (i.e., handwashing with soap and water or use of an alcohol-based hand rub) after contact with an influenza patient or the environment in which care is provided.
- Although no studies have assessed the use of masks at home to decrease the spread of infection, use of surgical or procedure masks by the patient and/or caregiver during interactions may be of benefit. The wearing of gloves and gowns is not recommended for household members providing care in the home.
- Soiled dishes and eating utensils should be washed either in a dishwasher or by hand with warm water and soap. Separation of eating utensils for use by a patient with influenza is not necessary.
- Laundry can be washed in a standard washing machine with warm or cold water and detergent. It is not necessary to separate soiled linen and laundry used by a patient with influenza from other household laundry. Care should be used when handling soiled laundry (i.e., avoid "hugging" the laundry) to avoid contamination. Hand hygiene should be performed after handling soiled laundry.
- Tissues used by the ill patient should be placed in a bag and disposed with other household waste. Consider placing a bag for this purpose at the bedside.
- Normal cleaning of environmental surfaces in the home should be followed.

H. Care of pandemic influenza patients at alternative sites

If an influenza pandemic results in severe illness that overwhelms the capacity of existing healthcare resources, it may become necessary to provide care at alternative sites (e.g., schools, auditoriums, conference centers, hotels). Existing "all-hazard" plans have likely identified designated sites for this purpose. The same principles of infection control apply in these settings as in other healthcare settings. Careful planning is necessary to ensure that resources are available and procedures are in place to adhere to the key principles of infection control.

S4-V. RECOMMENDATIONS FOR INFECTION CONTROL IN SCHOOLS AND WORKPLACES

- In schools and workplaces, infection control for pandemic influenza should focus on:
  - Keeping sick students, faculty, and workers away while they are infectious.
  - Promoting respiratory hygiene/cough etiquette and hand hygiene as for any respiratory infection.

  The benefit of wearing masks in these settings has not been established.

- School administrators and employers should ensure that materials for respiratory hygiene/cough etiquette (i.e., tissues and receptacles for their disposal) and hand hygiene are available. Educational messages and infection control guidance for pandemic influenza are available for distribution. (CDC will develop educational materials appropriate to various audiences.)

S4-VI. RECOMMENDATIONS FOR INFECTION CONTROL IN COMMUNITY SETTINGS

Infection control in the community should focus on "social distancing" and promoting respiratory hygiene/cough etiquette and hand hygiene to decrease exposure to others. This could include the use of masks by persons with respiratory symptoms, if feasible. Although the use of masks in community settings has not been demonstrated to be a public health measure to decrease infections during a community outbreak, persons may choose to wear a mask as part of individual protection strategies that include cough etiquette, hand hygiene, and avoiding public gatherings. Mask use may also be important for persons who are at high risk for complications of influenza. Public education should be provided on how to use masks appropriately. Persons at high risk for complications of influenza should try to avoid public gatherings (e.g., movies, religious services, public meetings) when pandemic influenza is in the community. They should also avoid going to other public areas (e.g., food stores, pharmacies); the use of other persons for shopping or home delivery service is encouraged.

BOX 1. SUMMARY OF INFECTION CONTROL RECOMMENDATIONS FOR CARE OF PATIENTS WITH PANDEMIC INFLUENZA

COMPONENT	RECOMMENDATIONS
STANDARD PRECAUTIONS	See www.cdc.gov/ncidod/hip/ISOLAT/std_prec_excerpt.htm
Hand hygiene	Perform hand hygiene after touching blood, body fluids, secretions, excretions, and contaminated items; after removing gloves; and between patient contacts. Hand hygiene includes both handwashing with either plain or antimicrobial soap and water or use of alcohol-based products (gels, rinses, foams) that contain an emollient and do not require the use of water. If hands are visibly soiled or contaminated with respiratory secretions, they should be washed with soap (either non-antimicrobial or antimicrobial) and water. In the absence of visible soiling of hands, approved alcohol-based products for hand disinfection are preferred over antimicrobial or plain soap and water because of their superior microbicidal activity, reduced drying of the skin, and convenience.
Personal protective equipment (PPE)	
• Gloves	• For touching blood, body fluids, secretions, excretions, and contaminated items; for touching mucous membranes and nonintact skin
• Gown	• During procedures and patient-care activities when contact of clothing/exposed skin with blood/body fluids, secretions, and excretions is anticipated
• Face/eye protection (e.g., surgical or procedure mask and goggles or a face shield)	• During procedures and patient care activities likely to generate splash or spray of blood, body fluids, secretions, excretions
Safe work practices	Avoid touching eyes, nose, mouth, or exposed skin with contaminated hands (gloved or ungloved); avoid touching surfaces with contaminated gloves and other PPE that are not directly related to patient care (e.g., door knobs, keys, light switches).
Patient resuscitation	Avoid unnecessary mouth-to-mouth contact; use mouthpiece, resuscitation bag, or other ventilation devices to prevent contact with mouth and oral secretions.
Soiled patient care equipment	Handle in a manner that prevents transfer of microorganisms to oneself, others, and environmental surfaces; wear gloves if visibly contaminated; perform hand hygiene after handling equipment.
Soiled linen and laundry	Handle in a manner that prevents transfer of microorganisms to oneself, others, and to environmental surfaces; wear gloves (gown if necessary) when handling and transporting soiled linen and laundry; and perform hand hygiene.
Needles and other sharps	Use devices with safety features when available; do not recap, bend, break or hand-manipulate used needles; if recapping is necessary, use a one-handed scoop technique; place used sharps in a puncture-resistant container.

BOX 1. SUMMARY OF INFECTION CONTROL RECOMMENDATIONS FOR CARE OF PATIENTS WITH PANDEMIC INFLUENZA (CONT.)

COMPONENT	RECOMMENDATIONS
STANDARD PRECAUTIONS (cont.)	See www.cdc.gov/ncidod/hip/ISOLAT/std_prec_excerpt.htm
Environmental cleaning and disinfection	Use EPA-registered hospital detergent-disinfectant; follow standard facility procedures for cleaning and disinfection of environmental surfaces; emphasize cleaning/disinfection of frequently touched surfaces (e.g., bed rails, phones, lavatory surfaces).
Disposal of solid waste	Contain and dispose of solid waste (medical and non-medical) in accordance with facility procedures and/or local or state regulations; wear gloves when handling waste; wear gloves when handling waste containers; perform hand hygiene.
Respiratory hygiene/cough etiquette Source control measures for persons with symptoms of a respiratory infection; implement at first point of encounter (e.g., triage/reception areas) within a healthcare setting.	Cover the mouth/nose when sneezing/coughing; use tissues and dispose in no-touch receptacles; perform hand hygiene after contact with respiratory secretions; wear a mask (procedure or surgical) if tolerated; sit or stand as far away as possible (more than 3 feet) from persons who are not ill.
DROPLET PRECAUTIONS	www.cdc.gov/ncidod/hip/ISOLAT/droplet_prec_excerpt.htm
Patient placement	Place patients with influenza in a private room or cohort with other patients with influenza.* Keep door closed or slightly ajar; maintain room assignments of patients in nursing homes and other residential settings; and apply droplet precautions to all persons in the room. *During the early stages of a pandemic, infection with influenza should be laboratory-confirmed, if possible.
Personal protective equipment	Wear a surgical or procedure mask for entry into patient room; wear other PPE as recommended for standard precautions.
Patient transport	Limit patient movement outside of room to medically necessary purposes; have patient wear a procedure or surgical mask when outside the room.
Other	Follow standard precautions and facility procedures for handling linen and laundry and dishes and eating utensils, and for cleaning/disinfection of environmental surfaces and patient care equipment, disposal of solid waste, and postmortem care.
AEROSOL-GENERATING PROCEDURES	During procedures that may generate small particles of respiratory secretions (e.g., endotracheal intubation, bronchoscopy, nebulizer treatment, suctioning), healthcare personnel should wear gloves, gown, face/eye protection, and a fit-tested N95 respirator or other appropriate particulate respirator.

BOX 2. RESPIRATORY HYGIENE/COUGH ETIQUETTE

To contain respiratory secretions, all persons with signs and symptoms of a respiratory infection, regardless of presumed cause, should be instructed to:

- Cover the nose/mouth when coughing or sneezing.
- Use tissues to contain respiratory secretions.
- Dispose of tissues in the nearest waste receptacle after use.
- Perform hand hygiene after contact with respiratory secretions and contaminated objects/materials.

Healthcare facilities should ensure the availability of materials for adhering to respiratory hygiene/cough etiquette in waiting areas for patients and visitors:

- Provide tissues and no-touch receptacles for used tissue disposal.
- Provide conveniently located dispensers of alcohol-based hand rub.
    - Provide soap and disposable towels for handwashing where sinks are available.

Masking and separation of persons with symptoms of respiratory infection

During periods of increased respiratory infection in the community, persons who are coughing should be offered either a procedure mask (i.e., with ear loops) or a surgical mask (i.e., with ties) to contain respiratory secretions. Coughing persons should be encouraged to sit as far away as possible (at least 3 feet) from others in common waiting areas. Some facilities may wish to institute this recommendation year-round.

supplement 5
clinical guidelines
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SUMMARY OF PUBLIC HEALTH ROLES AND RESPONSIBILITIES FOR CLINICAL GUIDELINES

INTERPANDEMIC AND PANDEMIC ALERT PERIODS

Healthcare providers:

- Be aware of case definitions; procedures for screening, infection control, and laboratory testing; and antiviral regimens for influenza A (H5N1) and other novel influenza viruses.
- Notify health departments about suspected/confirmed novel influenza cases and fatalities.
- Collect recommended specimens for diagnosis of novel influenza, and forward specimens to designated state and federal laboratories.

State and local public health agencies:

- Help educate healthcare providers about novel and pandemic influenza.
- Provide or facilitate testing and investigation of suspected novel influenza cases.
- Conduct follow-up of suspected novel influenza cases.

HHS agencies:

- Develop and disseminate recommendations on the use of influenza diagnostic tests, antiviral drugs, and vaccines during a pandemic (see also Supplement 6 and Supplement 7).
- Develop a national stockpile of antiviral drugs for use during a pandemic (see also Supplement 6).
- Work with partner organizations to discuss and resolve clinical issues related to pandemic influenza response.
- Assist ministries of health and WHO in characterizing cases of human infection with avian influenza A (H5N1) or other novel strains of influenza, particularly with regard to antiviral susceptibility, transmission parameters, and clinical outcomes.
- Work with state and local health departments to investigate and manage suspected cases of human infection with avian influenza A (H5N1) or other novel strains of influenza.
- Establish case definition and reporting mechanisms.

PANDEMIC PERIOD

Healthcare providers:

- Regularly consult updates on case definitions, screening, laboratory testing, and treatment algorithms for pandemic influenza.
- Report pandemic influenza cases or fatalities as requested by health departments.
- Collect recommended specimens for ongoing pandemic influenza surveillance, and forward specimens as requested to designated state and federal laboratories.
- Report atypical cases, breakthrough infections while on prophylaxis, or any other abnormal cases throughout the duration of the pandemic to public health agencies.

State and local public health agencies:

- Update providers regularly as the influenza pandemic unfolds.
- Provide or facilitate testing and investigation of pandemic influenza cases.
- Work with CDC to investigate and report special pandemic situations.

HHS responsibilities:

- Update and disseminate national guidelines on influenza diagnostic testing and use of antiviral drugs and vaccines during the pandemic.
- Develop a pandemic influenza vaccine (see also Part 1 and Supplement 6).
- Work with healthcare partners to refine clinical management guidelines and issue regular updates on treatment issues.
- Conduct observational and interventional studies with partner institutions to investigate pandemic influenza pathogenesis and develop disease prevention and treatment strategies.
- Monitor pandemic influenza cases for antiviral resistance and transmission parameters.
- Monitor antiviral drug use and inventories.
- Collect information on clinical features, outcomes, and treatments.

S5-I. RATIONALE

Healthcare providers play an essential role in the detection of an initial case of novel or pandemic influenza in a community. If implemented early, identification and isolation of cases may help slow the spread of influenza within a community. Clinical awareness of novel or pandemic influenza disease can also benefit the individual patient, as rapid diagnosis and initiation of treatment can avert potentially severe complications. Detection is complicated, however, by the lack of specific clinical findings and commercially available laboratory tests that can rapidly distinguish novel or pandemic influenza from seasonal influenza. In addition, neither the clinical characteristics of a novel or pandemic influenza virus strain nor the groups at highest risk for complications can necessarily be defined beforehand. Therefore, clinicians face significant challenges in: 1) quickly identifying and triaging cases, 2) containing the spread of infection, 3) beginning an efficient and comprehensive workup, 4) initiating antiviral and other supportive therapy, and 5) anticipating clinical complications.

S5-II. OVERVIEW

Supplement 5 provides clinical procedures for the initial screening, assessment, and management of patients with suspected novel influenza during the Interpandemic and Pandemic Alert Periods, and for patients with suspected pandemic influenza during the Pandemic Period. The Appendices include information on the clinical presentation and complications of seasonal influenza, the clinical features of infection due to avian influenza A (H5N1) virus and previous pandemic influenza viruses, and the management of patients with community-acquired pneumonia or secondary bacterial pneumonia during a pandemic. The guidance is current as of October 2005, and is subject to change as experience is gained. Updates will be provided, as needed, on the CDC website (www.cdc.gov/flu/).

During the Interpandemic and Pandemic Alert Periods, early recognition of illness caused by a novel influenza A virus strain will rely on a combination of clinical and epidemiologic features. During the Pandemic Period (in a setting of high community

prevalence), diagnosis will likely be more clinically oriented because the likelihood will be high that any severe febrile respiratory illness is pandemic influenza. During periods in which no human infections with a novel influenza A virus strain have occurred anywhere in the world (Interpandemic Period: Phases 1, 2; see Box 1), or when sporadic cases of animal-to-human transmission or rare instances of limited human-to-human transmission of a novel influenza A virus strain have occurred in the world (Pandemic Alert Period: Phases 3, 4), the likelihood of novel influenza A virus infection is very low in a returned traveler from an affected area who has severe respiratory disease or influenza-like illness. Since human influenza A and B viruses circulate worldwide among humans year-round, the possibility of infection with human influenza viruses is much higher and should be considered. Once local person-to-person transmission of a novel influenza A virus strain has been confirmed (Pandemic Alert Period: Phase 5), the potential for novel influenza A virus infection will be higher in an ill person who has a strong epidemiologic link to the affected area (Box 1).

This supplement is designed to serve as a guide for clinicians, with the understanding that the management of influenza is based primarily on sound clinical judgment regarding the individual patient as well as an assessment of locally available resources, such as rapid diagnostics, antiviral drugs, and hospital beds. Early antiviral therapy shortens the duration of illness due to seasonal influenza and would be expected to have similar effects on illness due to novel or pandemic influenza viruses (see **Supplement 7: Antiviral Drug Distribution and Use)**.[1]

Clinical management must also address supportive care and management of influenza-related complications.

Other supplements that cover topics of potential interest to clinicians:

Supplement 1. Pandemic Influenza Surveillance

Supplement 2. Laboratory Diagnostics

Supplement 3. Healthcare Planning

Supplement 4. Infection Control

Supplement 6. Vaccine Distribution and Use

Supplement 7. Antiviral Drug Distribution and Use

S5-III. CLINICAL GUIDELINES FOR THE INTERPANDEMIC AND PANDEMIC ALERT PERIODS

During the Interpandemic and Pandemic Alert Periods, the primary goal of rapid detection is to quickly identify and contain cases of novel influenza. To limit the need to evaluate an overwhelming number of patients, the screening criteria should be specific, relying on a combination of clinical and epidemiologic features. Although febrile respiratory illnesses are one of the most common indications for medical evaluation, particularly during the winter, during the interpandemic and pandemic alert period, human cases of novel influenza are expected to be quite rare; laboratory diagnosis will most likely be sought for those with severe respiratory illness, such as pneumonia. The main features of detection and clinical management during the Interpandemic and Pandemic Alert Periods are outlined in Figure 1.

A. Criteria for evaluation of patients with possible novel influenza

The following criteria are based on the features of recent avian influenza A (H5N1) cases but are intended for use in evaluating suspected cases of infection with any novel influenza A virus strain. During the Pandemic Alert Period, human infections with novel influenza A viruses will be an uncommon cause of influenza-like illness; therefore, **both clinical and epidemiologic criteria should be met**. The criteria will be updated when needed as more data are collected.

[1] Information on HHS recommendations on the use of limited stocks of antiviral medications during a pandemic is provided in **Supplement 7**.

1. Clinical criteria

Any suspected cases of human infection with a novel influenza virus must first meet the criteria for influenza-like illness (ILI), defined as temperature of >38°C plus either sore throat or cough. Since lower respiratory tract involvement might result in dyspnea (shortness of breath), dyspnea should be considered as an additional criterion. Therefore, the full clinical criteria are: **fever plus one of the following: sore throat, cough, or dyspnea**.

Although recent infections with novel influenza viruses have resulted in severe respiratory illness, the next pandemic influenza virus strain might present with a different clinical syndrome (see Appendix 1 and Appendix 2). In such a situation, the clinical criteria will be modified accordingly and posted at www.cdc.gov/flu.

Given the large number of influenza-like illnesses that clinicians encounter during a typical flu season, **laboratory evaluation** for novel influenza A viruses during the Interpandemic and Pandemic Alert Periods is recommended only for:

- Hospitalized patients with severe ILI, including pneumonia, who meet the epidemiologic criteria (see below), *or*
- Non-hospitalized patients with ILI **and** with strong epidemiologic suspicion of novel influenza virus exposure (e.g., direct contact with ill poultry in an affected area, or close contact with a known or suspected human case of novel influenza.). (See Appendix 2, Supplement 2: Laboratory Diagnostics)
- Recommendations for the evaluation of patients with respiratory illnesses are provided in Box 2. Exceptions to the current clinical criteria are provided in Box 3.

2. Epidemiologic criteria

Epidemiologic criteria for evaluation of patients with possible novel influenza focus on the risk of exposure to a novel influenza virus with pandemic potential. Although the incubation period for seasonal influenza ranges from 1 to 4 days, the incubation periods for novel types of influenza are currently unknown and might be longer. Therefore, the maximum interval between potential exposure and symptom onset is set conservatively at 10 days.

Exposure risks—Exposure risks fall into two categories: travel and occupational.

- **Travel risks**

  Persons have a travel risk if they have: 1) recently visited or lived in an area affected by highly pathogenic avian influenza A outbreaks in domestic poultry or where a human case of novel influenza has been confirmed, *and either* 2) had direct contact with poultry, or 3) had close contact with a person with confirmed or suspected novel influenza. Updated listings of areas affected by avian influenza A (H5N1) and other current/recent novel strains are provided on the websites of the OIE (http://www.oie.int/eng/en_index.htm), WHO (www.who.int/en/), and CDC (www.cdc.gov/flu/).

  Direct contact with poultry is defined as: 1) touching birds (well-appearing, sick, or dead), or 2) touching poultry feces or surfaces contaminated with feces, or 3) consuming uncooked poultry products (including blood) in an affected area. *Close contact* with a person from an infected area with confirmed or suspected novel influenza is defined as being within 3 feet (1 meter) of that person during their illness.

  Because specific testing for human infection with avian influenza A (H5N1) might not be locally available in an affected area, persons reporting close contact in an affected area with a person suffering from a severe, yet unexplained, respiratory illness should also be evaluated.

  Clinicians should recognize that human influenza viruses circulate worldwide and year-round, including in countries with outbreaks of avian influenza A (H5N1) among poultry. Therefore, during the Interpandemic and Pandemic Alert Periods, human influenza virus infection can be a cause of ILI among returned travelers at any time of the year, including during the summer in the United States. This includes travelers returning from areas affected by poultry outbreaks of highly pathogenic avian influenza A (H5N1) in Asia. As of October 2005, such persons are currently more likely to have infection with human influenza viruses than with avian influenza A (H5N1) viruses.

- **Occupational risks**

  Persons at occupational risk for infection with a novel strain of influenza include persons who work on farms or live poultry markets or who process or handle poultry infected with known or suspected avian influenza viruses, workers in laboratories that contain live animal or novel influenza viruses, and healthcare workers in direct contact with a suspected or confirmed novel influenza case.

  Information on limiting occupational risk is provided on the Occupational Health and Safety Administration (OSHA) website at: www.osha.gov/dsg/guidance/avian-flu.html.

  During the Interpandemic and Pandemic Alert Periods, when there is no sustained human-to-human transmission of any novel influenza viruses, **direct contact with animals such as poultry in an affected area or close contact with a case of suspected or confirmed human novel influenza**—for any reason—is required for further evaluation. During the Pandemic Alert Period, Phases 3 and 4, the majority of human cases of novel influenza will result from avian-to-human transmission (see Box 1). Therefore, a history of direct contact with poultry (well-appearing, sick, or dead), consumption of uncooked poultry or poultry products, or direct exposure to environmental contamination with poultry feces in an affected area will be important to ascertain. During the Pandemic Alert Period, Phase 5, a history of close contact with an ill person suspected or confirmed to have novel influenza in an affected area will be even more important.

  Other avian influenza A viruses — Although the epidemiologic criteria for novel influenza are based on recent human cases of avian influenza A (H5N1), they are intended for use in the evaluation of suspected cases of infection with any novel influenza A virus strain, including other avian influenza viruses. Other avian influenza A viruses that have caused human disease include the highly pathogenic viruses H7N7 and H7N3 and the low pathogenic viruses H9N2 and H7N2 (see Supplement 2, Box 3). Some of these human cases have occurred in Europe (Netherlands) and North America (Canada and the United States). Therefore, the same high-risk exposures defined above for avian influenza A (H5N1) also apply to other avian influenza A viruses. A strong epidemiologic link to an avian influenza outbreak in poultry—even in areas that have not experienced poultry outbreaks of avian influenza A (H5N1)—may raise the index of suspicion for human infection with avian influenza A viruses.

In the future, other animal hosts (in addition to poultry) or novel influenza A virus subtypes (in addition to H5N1) might become significantly associated with human disease. If such events occur, this guidance will be updated.

B. Initial management of patients who meet the criteria for novel influenza

When a patient meets **both the clinical and epidemiologic criteria** for a suspected case of novel influenza, healthcare personnel should initiate the following activities:

- **Implement infection control precautions** for novel influenza, including Respiratory Hygiene/Cough Etiquette. Patients should be placed on Droplet Precautions for a minimum of 14 days, unless there is full resolution of illness or another etiology has been identified before that period has elapsed. Healthcare personnel should wear surgical or procedure masks on entering a patient's room, as per Droplet Precautions, as well as gloves and gowns, when indicated for Standard Precautions (Table). Patients should be admitted to a single-patient room, and patient movement and transport within the hospital should be limited to medically necessary purposes (see also **Supplement 4**).
- **Notify the local and state health departments.** Report each patient who meets the clinical and epidemiologic criteria for a suspected case of novel influenza to the state or local health department as quickly as possible to facilitate initiation of public health measures (see **Supplement 1**). Designate one person as a point of contact to update public health authorities on the patient's clinical status.
- **Obtain clinical specimens for novel influenza A virus testing and notify the local and state health departments to arrange testing.** Testing will likely be directed by public health authorities; current guidelines are provided in **Supplement 2**. Since the optimal specimens for detecting novel influenza A virus infections are currently unknown, if feasible, **all** of the following respiratory specimens should be collected for novel influenza A virus testing:

nasopharyngeal swab; nasal swab, wash, or aspirate; throat swab; and tracheal aspirate (for intubated patients). Store specimens at 4°C in viral transport media until transported or shipped for testing. Acute (within 7 days of illness onset) and convalescent serum specimens (2–3 weeks after the acute specimen and at least 3 weeks after illness onset) should be obtained and refrigerated at 4°C or frozen at minus 20–80°C. Serological testing for novel influenza virus infection can be performed only at CDC.

Clinicians should immediately notify their local health departments of their intention to ship clinical specimens from suspected cases of human infection with avian influenza, to ensure that the specimens are handled under proper biocontainment conditions (see **Supplement 2**).

Novel influenza can be confirmed by RT-PCR or virus isolation from tissue cell culture with subtyping. RT-PCR for testing of novel influenza viruses cannot be performed by a hospital laboratory and is available only at state public health laboratories and CDC. **Viral culture of specimens from suspected novel influenza cases should be attempted only in laboratories that meet the biocontainment conditions for BSL-3 with enhancements or higher.**

Rapid influenza diagnostic tests and immunofluorescence (indirect fluorescent antibody staining [IFA] or direct fluorescent antibody staining [DFA]) may be used to detect seasonal influenza, but **should not be used to confirm or exclude novel influenza during the Pandemic Alert Period**. Rapid influenza tests have relatively low sensitivity for detecting seasonal influenza,[2] and their ability to detect novel influenza subtypes is unknown. The sensitivity of rapid diagnostic tests will likely be higher in specimens collected within two days of illness onset, in children, and when tested in clinical laboratories that perform a high volume of testing. Such tests can identify influenza A viruses but cannot distinguish between human infection with seasonal and novel influenza A viruses. A negative rapid influenza test result does not necessarily exclude human infection with either seasonal or novel influenza A viruses. A positive rapid influenza test result could be a false positive or represent infection with either seasonal or novel influenza A viruses. Therefore, both negative and positive rapid influenza test and immunofluoresence results should be interpreted with caution, and RT-PCR testing for influenza viruses should be performed. Further information on rapid diagnostic testing is provided in **Supplement 2**.

Acute and convalescent serum samples and other available clinical specimens (respiratory, blood, and stool) should be saved and refrigerated or frozen for additional testing until a specific diagnosis is made.

- **Evaluate alternative diagnoses.** An alternative diagnosis should be based only on laboratory tests with high positive-predictive value (e.g., blood culture, viral culture, PCR, *Legionella* urinary antigen, pleural fluid culture, transthoracic aspirate culture). If an alternate etiology is identified, the possibility of co-infection with a novel influenza virus may still be considered if there is a strong epidemiologic link to exposure to novel influenza.
- **Decide on inpatient or outpatient management.** The decision to hospitalize a suspected novel influenza case will be based on the physician's clinical assessment and assessment of risk and whether adequate precautions can be taken at home to prevent the potential spread of infection. Patients cared for at home should be separated from other household members as much as possible. All household members should carefully follow recommendations for hand hygiene, and tissues used by the ill patient should be placed in a bag and disposed with other household waste (Box 4). Although no studies have assessed the use of masks at home to decrease the spread of infection, use of surgical or procedure masks by the patient and/or caregiver during interactions may be of benefit.Separation of eating utensils for use by a patient with influenza is not necessary, as long as they are washed with warm water and soap (Box 4).
- **Initiate antiviral treatment** as soon as possible, even if laboratory results are not yet available. Clinical trials have shown that these drugs can decrease the illness due to seasonal influenza duration by several days when they are initiated within 48 hours of illness onset. The clinical effectiveness of antiviral drugs for treatment of novel influenza is unknown, but it is likely that the earlier treatment is initiated, the greater the likelihood of benefit. During the

[2] Uyeki TM. Influenza diagnosis and treatment in children: a review of studies on clinically useful tests and antiviral treatment for influenza. Pediatr Infect Dis J. 2003 Feb;22(2):164-77.

Pandemic Alert Period, available virus isolates from any case of novel influenza will be tested for resistance to the currently licensed antiviral medications. See **Supplement 7** for current antiviral information and treatment strategies.

- **Assist public health officials with the identification of potentially exposed contacts.** After consulting with state and local public health officials, clinicians might be asked to help identify persons exposed to the suspected novel influenza case-patient (particularly healthcare workers). In general, persons in close contact with the case-patient at any time beginning one day before the onset of illness are considered at risk. Close contacts might include household and social contacts, family members, workplace or school contacts, fellow travelers, and/or healthcare providers (see **Supplement 8** and **Supplement 9**).

C. Management of patients who test positive for novel influenza

If a patient is confirmed to have an infection with a novel influenza virus, healthcare personnel should continue antiviral treatment and all isolation and infection control precautions, and isolate patients with novel influenza from seasonal influenza patients. In addition to prior vaccination against seasonal influenza, such measures may decrease the risk of co-infection and viral genetic reassortment.

D. Management of patients who test positive for seasonal influenza

Many suspected novel influenza cases may be found to have seasonal human influenza, particularly during the winter season. It should be recognized that **human influenza viruses circulate among people worldwide, including in affected areas with poultry outbreaks of avian influenza A viruses during non-seasonal influenza activity in the United States**. For patients with confirmed seasonal influenza, maintain Standard and Droplet Precautions, and continue antiviral treatment for a full treatment course (e.g., 5 days).

E. Management of patients who test negative for novel influenza

The sensitivity of the currently available tests for detecting novel influenza viruses in clinical specimens has not been thoroughly evaluated with a full range of specimen types. Consequently, false-negative test results may occur. Therefore, if test results are negative but the clinical and epidemiologic suspicion remains high, continuing antiviral treatment and isolation procedures should be considered. Test results might be negative for influenza viruses for several reasons. Some patients might have an alternate etiology to explain their illness. The general work-up for febrile respiratory illnesses described below should evaluate the most common alternate causes. A certain number of truly infected cases might also test falsely negative, due to specimen collection conditions, to viral shedding that is not detectable, or to sensitivity of the test. Interpretation of negative testing results should be tailored to the individual patient in consultation with hospital infection control and infectious disease specialists, as well as the state or local health department and CDC. In hospitalized patients who test negative for novel influenza but have no alternate diagnosis established, novel-influenza-directed management should be continued if clinical suspicion is high and there is a strong epidemiologic link to exposure to novel influenza. When influenza tests are negative and an alternative diagnosis is established, isolation precautions and antiviral drug therapy for novel influenza may be discontinued based on clinician's assessment, particularly in the absence of a strong epidemiologic link, if the alternative diagnosis is made using a test with a high positive-predictive value, and if the clinical manifestations are explained by the alternative diagnosis.

S5-IV. CLINICAL GUIDELINES FOR THE PANDEMIC PERIOD

During the Pandemic Period, the primary goal of rapid detection is to appropriately identify and triage cases of pandemic influenza. During this period, outpatient clinics and emergency departments might be overwhelmed with suspected cases, restricting the time and laboratory resources available for evaluation. In addition, if the pandemic influenza virus exhibits transmission characteristics similar to those of seasonal influenza viruses, illnesses will likely spread throughout the community too rapidly to allow the identification of obvious exposures or contacts. Evaluation will therefore focus predominantly on clinical and basic laboratory findings, with less emphasis on laboratory diagnostic testing (which may be in

short supply) and epidemiologic criteria. Nevertheless, clinicians in communities without pandemic influenza activity might consider asking patients about recent travel from a community with pandemic influenza activity or close contact with a suspected or confirmed pandemic influenza case. The main features of clinical management during the Pandemic Period are outlined in Figure 2.

A. Criteria for evaluation of patients with possible pandemic influenza

1. Clinical criteria

Suspected cases of pandemic influenza virus infection should meet the criteria for ILI: temperature of >38°C plus either sore throat or cough. Since lower respiratory tract involvement might result in dyspnea (shortness of breath), dyspnea should be considered as an additional criterion. Therefore, the full clinical criteria are: **fever plus one of the following: sore throat, cough, or dyspnea.** Although past influenza pandemics have most frequently resulted in respiratory illness, the next pandemic influenza virus strain might present with a different clinical syndrome (see Appendix 1 and Appendix 2). During a pandemic, updates on other clinical presentations will be provided at: www.pandemicflu.gov and www.cdc.gov/flu/.

Recommendations for general evaluation of patients with influenza-like illness are provided in Box 2. Exceptions to the clinical criteria are provided in Box 3.

2. Epidemiologic criteria

During the Pandemic Period, an exposure history will be marginally useful for clinical management when disease is widespread in a community. In addition, there will be a relatively high likelihood that any case of ILI during that time period will be pandemic influenza. Once pandemic influenza has arrived in a particular locality, clinical criteria will be sufficient for classifying the patient as a suspected pandemic influenza case.

B. Initial management of patients who meet the criteria for pandemic influenza

When a patient meets the criteria for a suspected case of pandemic influenza, healthcare personnel should initiate the following activities:

- **Follow local and state health department recommendations on reporting** for patients who meet the criteria for pandemic influenza. See **Supplement 1** for guidance on case reporting during the Pandemic Period.
- **If the patient is hospitalized, implement infection control precautions for pandemic influenza,** including Respiratory Hygiene/Cough Etiquette (see Table and **Supplement 4**). Place the patient on Droplet Precautions for a minimum of **5 days** from the onset of symptoms. Healthcare personnel should wear surgical or procedure masks on entering a patient's room, as per Droplet Precautions, as well as gloves and gowns when indicated, as per Standard Precautions (Table). Once a pandemic is underway, hospital admission of patients should be limited to those with severe complications who cannot be cared for outside the hospital setting. Patients should be admitted to either a single-patient room or an area designated for cohorting of patients with influenza. Patient movement and transport outside the isolation area should be limited to medically necessary purposes (see Table).
- **Obtain clinical specimens** for general evaluation, as clinically indicated (see Box 2). Once pandemic influenza has arrived in a community, influenza testing will likely not be needed for most patients. Laboratory testing in conjunction with health departments will likely be performed in a subset of pandemic influenza cases, however, as part of ongoing virologic surveillance to monitor the antigenic evolution of the strains for vaccine strain selection purposes (see **Supplement 1**). At the beginning or end of a pandemic outbreak in a community, diagnostic testing might aid cohorting decisions, but may be optional in the setting of high local prevalence. Influenza diagnostic testing should be considered before initiating treatment with antivirals (see **Supplement 7**). Guidelines for pandemic influenza virus testing are provided in **Supplement 2**.

As with seasonal influenza, RT-PCR and virus isolation from tissue culture will be the most accurate methods for diagnosing pandemic influenza. Generally, specimens should include combined nasopharyngeal aspirates or nasal swabs, and throat swabs, stored at 4°C in viral transport media. During the Pandemic Period, BSL-2 conditions should be sufficient for viral culture of clinical specimens from suspected pandemic influenza patients.

Rapid diagnostic tests for influenza and immunofluoresence may be helpful for initial clinical management, including cohorting and treatment (see above). However, rapid influenza tests have relatively low sensitivity for detecting seasonal influenza, and their ability to detect pandemic influenza viruses is unknown. The sensitivity of rapid diagnostic tests will likely be higher in specimens collected within two days of illness onset, in children, and when tested at clinical laboratories that perform a high volume of testing. Because during a pandemic a negative rapid test may be a false negative, test results need to be interpreted within the overall clinical context. For example, it may not be optimal to withhold antiviral treatment from a seriously ill high risk patient on the basis of a negative test; however, in a setting of limited antiviral drug availability, treatment decisions in less high risk situations could be based on test results. The risk of a false-negative test also must be taken into account in making cohorting decisions. Rapid diagnostic testing should not preclude more reliable testing, if available. Further information on rapid diagnostic testing can be found in **Supplement 2**.

- **Decide on inpatient or outpatient management.** The decision to hospitalize a suspected pandemic influenza case will be based on the physician's clinical assessment of the patient as well as the availability of hospital beds and personnel. Guidelines on cohorting and infection control for admitted patients can be found in **Supplement 3** and **Supplement 4**.

  An unstable patient will be considered a high priority for admission, but patients with high-risk conditions (see Appendix 1) might also warrant special attention, such as observation or close follow-up, even if disease is mild. On the other hand, home management with follow-up might be appropriate for well-appearing young children with fever alone. See **Supplement 7** for inpatient and outpatient treatment strategies.

  Patients cared for at home should be separated from other household members as much as possible. All household members should carefully follow recommendations for hand hygiene, and tissues used by the ill patient should be placed in a bag and disposed with other household waste (Box 4). Infection within the household may be minimized if a primary caregiver is designated; ideally, someone who does not have an underlying condition that places them at increased risk of severe influenza disease. Although no studies have assessed the use of masks at home to decrease the spread of infection, using a surgical or procedure mask by the patient or caregiver during interactions may be of benefit. Separation of eating utensils for use by a patient with influenza is not necessary, as long as they are washed with warm water and soap (Box 4).

C. Clinical management of pandemic influenza patients

See **Supplement 7** for current antiviral information and treatment strategies.[3] In addition to use of antivirals, clinical management of severe influenza should address supportive care and the rapid identification and treatment of secondary complications. During the Pandemic Period, CDC may request virus isolates from persons who fail treatment or antiviral prophylaxis, as these strains may more likely be drug resistant. In addition, randomly collected isolates will be tested for resistance to establish nationwide rates (see **Supplement 1**).

Children aged <18 years with suspected or confirmed pandemic influenza should not be treated with aspirin or other salicylate-containing products because of an increased risk of Reye syndrome (characterized by acute encephalopathy and liver failure) in this age group.

[3] Ribavirin and immunomodulatory therapies, such as steroids, are not approved by the FDA for treatment of severe influenza of any type and are purely investigational at this time. These agents frequently have severe adverse effects, such as bone marrow and hepatic toxicity, while the benefits of these therapies are unknown.

The major clinical presentations and complications related to seasonal human influenza occur more commonly in persons with certain underlying medical conditions, such as chronic respiratory or cardiovascular disease and extremes of age, and are described in Appendix 1. Limited data are available on risk factors and complications related to infection with novel influenza viruses, and these may change as individual strains evolve. A summary of the clinical presentations and complications associated with recent influenza A (H5N1) viruses is included in Appendix 2. In particular, post-influenza community-acquired pneumonia will likely be a commonly encountered complication, and clinicians will need to be aware of recommended methods for diagnosis and treatment. Guidance on the management of influenza-related pneumonia is presented in Appendix 3.

BOX 1. RISK OF NOVEL INFLUENZA IN PERSONS WITH SEVERE RESPIRATORY DISEASE OR INFLUENZA-LIKE ILLNESS DURING THE INTERPANDEMIC AND PANDEMIC ALERT PERIODS

Clinicians should recognize that human influenza A and B viruses and other respiratory viruses circulate year-round among people throughout the world, including in countries affected by outbreaks of avian influenza A viruses in poultry. Seasonal human influenza A and B community outbreaks occur in temperate climates of the northern and southern hemisphere, and human influenza activity may occur year-round in subtropical and tropical regions. Outbreaks of human influenza can occur among travelers during any time of the year, including periods of low influenza activity in the United States (e.g., summer).

Phases 1, 2: Interpandemic Period

A novel influenza A virus has been detected in animals but not in humans. **During these phases, the risk of human infection with a novel influenza A virus strain is extremely low. The risk of human infection with human influenza viruses or other viruses is much higher in persons living in or traveling to affected areas.**

Phases 3, 4: Pandemic Alert Period

A novel influenza A virus has been detected in humans through sporadic animal-to-human transmission in an affected area (e.g., direct contact with infected poultry), and few cases of limited, local human-to-human transmission have occurred (small clusters of cases). **During these phases, the risk of human infection with a novel influenza A virus strain is very low. The risk of human infection with human influenza viruses or other viruses is much higher in persons living in or traveling to affected areas.**

Phase 5: Pandemic Alert Period

A novel influenza A virus has been detected in humans in larger clusters in an affected area, suggesting that the virus is becoming better adapted to spread among people. **During this period, the risk of human infection with a novel influenza A virus strain is higher, depending on specific exposures, in persons living in or traveling to affected areas. Human infection with human influenza viruses or other viruses will occur and should still be considered.**

BOX 2. CLINICAL EVALUATION OF PATIENTS WITH INFLUENZA-LIKE ILLNESS DURING THE INTERPANDEMIC AND PANDEMIC ALERT PERIODS

- Patients who require hospitalization for an influenza-like illness for which a definitive alternative diagnosis is not immediately apparent* should be questioned about: 1) travel to an area affected by avian influenza A virus outbreaks in poultry, 2) direct contact with poultry, 3) close contact with persons with suspected or confirmed novel influenza, or 4) occupational exposure to novel influenza viruses (such as through agricultural, health care, or laboratory activities).
- Patients may be screened on admission for recent seasonal influenza vaccination and pneumococcal vaccination. Those without a history of immunization should receive these vaccines before discharge, if indicated.
- Patients meeting the epidemiologic criteria for possible infection with a novel strain of influenza should undergo a routine diagnostic work-up, guided by clinical indications. Appropriate personal protective equipment should be used when evaluating patients with suspected novel influenza, including during collection of specimens.**
- Diagnostic testing for a novel influenza A virus should be initiated as follows:
  - Collect **all** of the following specimens: nasopharyngeal swab, nasal swab, wash, or aspirate, throat swab, and tracheal aspirate (if intubated), and place into viral transport media and refrigerate at 4° C until specimens can be transported for testing.
  - Immediately contact the local and state health departments to report the suspected case and to arrange novel influenza testing by RT-PCR..

  RT-PCR testing is not available in hospital laboratories and must be performed at a qualified laboratory such as a state health department laboratory or the CDC Influenza Laboratory. **Viral culture should be performed only at biosafety level 3 [BSL-3] with enhancements (see Supplement 2).**
- Depending on the clinical presentation and the patient's underlying health status, other initial diagnostic testing might include:
  - Pulse oximetry
  - Chest radiograph
  - Complete blood count (CBC) with differential
  - Blood cultures
  - Sputum (in adults), tracheal aspirate, and pleural effusion aspirate (if an effusion is present) Gram stain and culture
  - Antibiotic susceptibility testing (encouraged for all bacterial isolates)
  - Multivalent immunofluorescent antibody testing or PCR of nasopharyngeal aspirates or swabs for common viral respiratory pathogens, such as influenza A and B, adenovirus, parainfluenza viruses, and respiratory syncytial virus, particularly in children
  - In adults with radiographic evidence of pneumonia, *Legionella* and pneumococcal urinary antigen testing
  - If clinicians have access to rapid and reliable testing (e.g., PCR) for *M. pneumoniae* and *C. pneumoniae*, adults and children <5 yrs with radiographic pneumonia should be tested.
  - Comprehensive serum chemistry panel, if metabolic derangement or other end-organ involvement, such as liver or renal failure, is suspected

*Further evaluation and diagnostic testing should also be considered for outpatients with strong epidemiologic risk factors and mild or moderate illness (see Box 3).

Healthcare personnel should wear surgical or procedure masks on entering a patient's room (Droplet Precautions), as well as gloves and gowns, when indicated (Standard Precautions) (see Table and **Supplement 4).

BOX 3. SPECIAL SITUATIONS AND EXCEPTIONS TO THE CLINICAL CRITERIA

Persons with a high risk of exposure—For persons with a high risk of exposure to a novel influenza virus (e.g., poultry worker from an affected area,* caregiver of a patient with laboratory-confirmed novel influenza, employee in a laboratory that works with live novel influenza viruses), epidemiologic evidence might be enough to initiate further measures, even if clinical criteria are not fully met. In these persons, early signs and symptoms—such as rhinorrhea, conjunctivitis, chills, rigors, myalgia, headache, and diarrhea—in addition to cough or sore throat, may be used to fulfill the clinical criteria for evaluation.

High-risk groups with atypical symptoms—Young children, elderly patients, patients in long-term care facilities, and persons with underlying chronic illnesses might not have typical influenza-like symptoms, such as fever. When such patients have a strong epidemiologic risk factor, novel influenza should be considered with almost any change in health status, even in the absence of typical clinical features. Conjunctivitis has been reported in patients with influenza A (H7N7) and (H7N3) infections. In young children, gastrointestinal manifestations such as vomiting and diarrhea might be present. Infants may present with fever or apnea alone, without other respiratory symptoms, and should be evaluated if there is an otherwise increased suspicion of novel influenza.

*Updated lists of affected areas are provided at the websites of the OIE (http://www.oie.int/eng/en_index.htm), WHO (www.who.int/en/), and CDC (www.cdc.gov/flu/).

BOX 4. HOME CARE INFECTION CONTROL GUIDANCE FOR PANDEMIC INFLUENZA PATIENTS AND HOUSEHOLD MEMBERS

Most patients with pandemic influenza will be able to remain at home during the course of their illness and can be cared for by family members or others who live in the household. Anyone who has been in the household with an influenza patient during the incubation period is at risk for developing influenza. A key objective in this setting is to limit transmission of pandemic influenza within and outside the home.

Management of influenza patients in the home

- Physically separate the patient with influenza from non-ill persons living in the home as much as possible.
- Patients should not leave the home during the period when they are most likely to be infectious to others (i.e., 5 days after onset of symptoms). When movement outside the home is necessary (e.g., for medical care), the patient should follow respiratory hygiene/cough etiquette (i.e., cover the mouth and nose when coughing and sneezing) and should wear a mask.

Management of other persons in the home

- Persons who have not been exposed to pandemic influenza and who are not essential for patient care or support should not enter the home while persons are still having a fever due to pandemic influenza.
- If unexposed persons must enter the home, they should avoid close contact with the patient.
- Persons living in the home with the patient with pandemic influenza should limit contact with the patient to the extent possible; consider designating one person as the primary care provider.
- Household members should be vigilant for the development of influenza symptoms. Consult with healthcare providers to determine whether a pandemic influenza vaccine, if available, or antiviral prophylaxis should be considered.

Infection control measures in the home

- All persons in the household should carefully follow recommendations for hand hygiene (i.e., hand washing with soap and water or use of an alcohol-based hand rub) after contact with an influenza patient or the environment in which they are receiving care.
- Although no studies have assessed the use of masks at home to decrease the spread of infection, using a surgical or procedure mask by the patient or caregiver during interactions may be beneficial.
- Soiled dishes and eating utensils should be washed either in a dishwasher or by hand with warm water and soap. Separation of eating utensils for use by a patient with influenza is not necessary.
- Laundry may be washed in a standard washing machine with warm or cold water and detergent. It is not necessary to separate soiled linen and laundry used by a patient with influenza from other household laundry. Care should be used when handling soiled laundry (i.e., avoid "hugging" the laundry) to avoid self-contamination. Hand hygiene should be performed after handling soiled laundry.
- Tissues used by the ill patient should be placed in a bag and disposed of with other household waste. Consider placing a bag for this purpose at the bedside.
- Environmental surfaces in the home should be cleaned using normal procedures.

FIGURE 1. CASE DETECTION AND CLINICAL MANAGEMENT DURING THE INTERPANDEMIC AND PANDEMIC ALERT PERIODS

Situation: No human cases of novel influenza are present in the community. Human cases might be present in another country or another region of the United States.

CLINICAL CRITERIA

An illness with **all** of the following:

- Temperature >38° C, *and*
- Cough, sore throat, or dyspnea, *and*
- Requiring hospitalization; or nonhospitalized with epidemiological link[1]

→ If no to **any**, treat as clinically indicated, but reevaluate if suspicion

AND

EPIDEMIOLOGIC CRITERIA

The clinician should ask the patient about the following **within 10 days** of symptom onset:

- History of recent **travel** to an affected area[2] **and** at least one of the following:
  - Direct contact with poultry or poultry products[3], *or*
  - Close contact with a person with suspected or confirmed novel influenza[4], *or*
  - Close contact with a person who died or was hospitalized due to a severe respiratory illness[3]
- Employment in an **occupation** at particular risk for novel influenza exposure, such as:
  - A health care worker in direct contact with a suspected or confirmed novel influenza case, *or*
  - A worker in a laboratory that contains live novel influenza virus, *or*
  - A worker in a poultry farm, live poultry market, or poultry processing operation with known or suspected avian influenza infection

→ If **no** to **both** criteria, treat as clinically indicated, but re-evaluate if suspicion

If **yes** to **either** criterion

- Initiate Standard and Droplet Precautions[5]
- Treat as clinically indicated[6]
- Notify state or local health department about the case[7]
- Initiate general work-up as clinically indicated[8]
- Collect and send specimens for novel influenza virus testing to the state health department or CDC[9]
- Begin empiric antiviral treatment[10]
- Help identify contacts, including HCWs[11]

Novel influenza positive by culture or RT-PCR

- Continue Standard and Droplet Precautions[5]
- Continue antivirals[10]
- Do not cohort with seasonal influenza patients
- Treat complications, such as secondary bacterial pneumonia, as indicated[13]
- Provide clinical updates to health department

All influenza testing negative[12]

- Continue infection control precautions, as clinically appropriate[5]
- Treat complications, such as secondary bacterial pneumonia, as indicated[13]
- Consider discontinuing antivirals, if considered appropriate[10]

Seasonal influenza positive by culture or RT-PCR

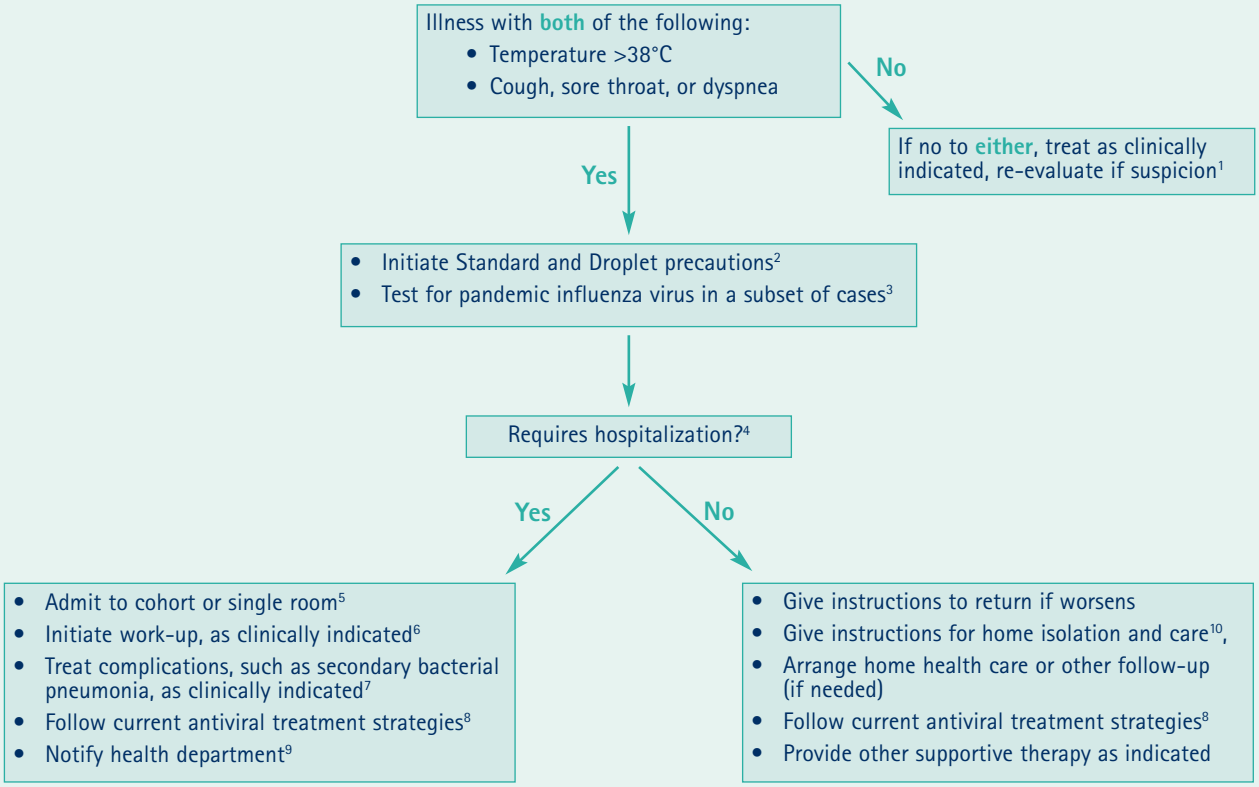
- Continue Standard and Droplet Precautions[5]
- Continue antivirals for a minimum of 5 days[10]
- Treat complications, such as secondary bacterial pneumonia, as indicated[13]

Footnotes to Figure 1:

1. Further evaluation and diagnostic testing should also be considered for outpatients with strong epidemiologic risk factors and mild or moderate illness. (See Box 2).
2. Updated information on areas where novel influenza virus transmission is suspected or documented is available on the CDC website at www.cdc.gov/travel/other/avian_flu_ah5n1_031605.htm and on the WHO website at www.who.int/en/.
3. For persons who live in or visit affected areas, close contact includes touching live poultry (well-appearing, sick or dead) or touching or consuming uncooked poultry products, including blood. For animal or market workers, it includes touching surfaces contaminated with bird feces. In recent years, most instances of human infection with a novel influenza A virus having pandemic potential, including influenza A (H5N1), are thought to have occurred through direct transmission from domestic poultry. A small number of cases are also thought to have occurred through limited person-to-person transmission or consumption of uncooked poultry products. Transmission of novel influenza viruses from other infected animal populations or by contact with fecally contaminated surfaces remains a possibility. These guidelines will be updated as needed if alternate sources of novel influenza viruses are suspected or confirmed.
4. Close contact includes direct physical contact, or approach within 3 feet (1 meter) of a person with suspected or confirmed novel influenza.
5. Standard and Droplet Precautions should be used when caring for patients with novel influenza or seasonal influenza (Table and **Supplement 4**). Information on infection precautions that should be implemented for all respiratory illnesses (i.e., Respiratory Hygiene/Cough Etiquette) is provided at: www.cdc.gov/flu/professionals/infectioncontrol/resphygiene.htm
6. Hospitalization should be based on all clinical factors, including the potential for infectiousness and the ability to practice adequate infection control. If hospitalization is not clinically warranted, and treatment and infection control is feasible in the home, the patient may be managed as an outpatient. The patient and his or her household should be provided with information on infection control procedures to follow at home (Box 3). The patient and close contacts should be monitored for illness by local public health department staff.
7. Guidance on how to report suspected cases of novel influenza is provided in **Supplement 1**.
8. The general work-up should be guided by clinical indications. Depending on the clinical presentation and the patient's underlying health status, initial diagnostic testing might include:
   - Pulse oximetry
   - Chest radiograph
   - Complete blood count (CBC) with differential
   - Blood cultures
   - Sputum (in adults), tracheal aspirate, pleural effusion aspirate (if pleural effusion is present) Gram stain and culture
   - Antibiotic susceptibility testing (encouraged for all bacterial isolates)
   - Multivalent immunofluorescent antibody testing or PCR of nasopharyngeal aspirates or swabs for common viral respiratory pathogens, such as influenza A and B, adenovirus, parainfluenza viruses, and respiratory syncytial virus, particularly in children
   - In adults with radiographic evidence of pneumonia, *Legionella* and pneumococcal urinary antigen testing
   - If clinicians have access to rapid and reliable testing (e.g., PCR) for *M. pneumoniae* and *C. pneumoniae*, adults and children <5 yrs with radiographic pneumonia should be tested.
   - Comprehensive serum chemistry panel, if metabolic derangement or other end-organ involvement, such as liver or renal failure, is suspected

   See Box 2 for additional details.
9. Guidelines for novel influenza virus testing can be found in **Supplement 2**. All of the following respiratory specimens should be collected for novel influenza A virus testing: nasopharyngeal swab; nasal swab, wash, or aspirate; throat swab; and tracheal aspirate (for intubated patients), stored at 4°C in viral transport media; and acute and convalescent serum samples.
10. Strategies for the use of antiviral drugs are provided in **Supplement 7**.
11. Guidelines for the management of contacts in a healthcare setting are provided in **Supplement 3**.
12. Given the unknown sensitivity of tests for novel influenza viruses, interpretation of negative results should be tailored to the individual patient in consultation with the local health department. Novel influenza directed management may need to be continued, depending on the strength of clinical and epidemiologic suspicion. Antiviral therapy and isolation precautions for novel influenza may be discontinued on the basis of an alternative diagnosis. The following criteria may be considered for this evaluation:
    - Absence of strong epidemiologic link to known cases of novel influenza
    - Alternative diagnosis confirmed using a test with a high positive-predictive value
    - Clinical manifestations explained by the alternative diagnosis
13. Guidance on the evaluation and treatment of suspected post-influenza community-associated pneumonia is provided in Appendix 3.

FIGURE 2. CASE DETECTION AND CLINICAL MANAGEMENT DURING THE PANDEMIC PERIOD


Illness with both of the following:
• Temperature >38°C
• Cough, sore throat, or dyspnea
No
If no to either, treat as clinically indicated, re-evaluate if suspicion[1]
Yes
• Initiate Standard and Droplet precautions[2]
• Test for pandemic influenza virus in a subset of cases[3]
Requires hospitalization?[4]
Yes
No
• Admit to cohort or single room[5]
• Initiate work-up, as clinically indicated[6]
• Treat complications, such as secondary bacterial pneumonia, as clinically indicated[7]
• Follow current antiviral treatment strategies[8]
• Notify health department[9]
• Give instructions to return if worsens
• Give instructions for home isolation and care[10],
• Arrange home health care or other follow-up (if needed)
• Follow current antiviral treatment strategies[8]
• Provide other supportive therapy as indicated

Situation: Pandemic influenza viruses are circulating in the community.

Footnotes to Figure 2:

1. Antiviral therapy and isolation precautions for pandemic influenza should be discontinued on the basis of an alternative diagnosis only when both the following criteria are met:
   - Alternative diagnosis confirmed using a test with a high positive-predictive value, and
   - Clinical manifestations entirely explained by the alternative diagnosis
2. Standard and Droplet Precautions should be used when caring for patients with novel influenza or seasonal influenza (Table and **Supplement 4**). Information on infection precautions that should be implemented for all respiratory illnesses (i.e., Respiratory Hygiene/Cough Etiquette) is provided at: www.cdc.gov/flu/professionals/infectioncontrol/resphygiene.htm
3. Guidance on laboratory testing during the Pandemic Period can be found in **Supplement 2**. Generally, specimens should include respiratory samples (e.g., nasopharyngeal wash/aspirate; nasopharyngeal, nasal or oropharyngeal swabs, or tracheal aspirates) stored at 4°C in viral transport media.

Routine laboratory confirmation of clinical diagnoses will be unnecessary as pandemic activity becomes widespread in a community. CDC will continue to work with state health laboratories to conduct virologic surveillance to monitor antigenic changes and antiviral resistance in the pandemic virus strains throughout the Pandemic Period.

4. The decision to hospitalize should be based on a clinical assessment of the patient and the availability of hospital beds and personnel.
5. Guidelines on cohorting can be found in **Supplement 4**. Laboratory confirmation of influenza infection is recommended when possible before cohorting patients.
6. The general work-up should be guided by clinical indications. Depending on the clinical presentation and the patient's underlying health status, initial diagnostic testing might include:
   - Pulse oximetry
   - Chest radiograph
   - Complete blood count (CBC) with differential
   - Blood cultures
   - Sputum (in adults) or tracheal aspirate Gram stain and culture
   - Antibiotic susceptibility testing (encouraged for all bacterial isolates)
   - Multivalent immunofluorescent antibody testing of nasopharyngeal aspirates or swabs for common viral respiratory pathogens, such as influenza A and B, adenovirus, parainfluenza viruses, and respiratory syncytial virus, particularly in children
   - In adults with radiographic evidence of pneumonia, *Legionella* and pneumococcal urinary antigen testing
   - If clinicians have access to rapid and reliable testing (e.g., PCR) for *M. pneumoniae* and *C. pneumoniae*, adults and children <5 yrs with radiographic pneumonia should be tested.
   - Comprehensive serum chemistry panel, if metabolic derangement or other end-organ involvement, such as liver or renal failure, is suspected

   See Box 2 for additional details.
7. Guidance on the evaluation and treatment of community acquired pneumonia and suspected post-influenza community-acquired bacterial pneumonia are provided in Appendix 3.
8. Strategies for the use of antiviral drugs are provided in **Supplement 7**.
9. Guidance on the reporting of pandemic influenza cases is provided in **Supplement 1**.
10. Patients with mild disease should be provided with standardized instructions on home management of fever and dehydration, pain relief, and recognition of deterioration in status. Patients should also receive information on infection control measures to follow at home (Box 4). Patients cared for at home should be separated from other household members as much as possible. All household members should carefully follow recommendations for hand hygiene, and tissues used by the ill patient should be placed in a bag and disposed of with other household waste. Infection within the household may be minimized if a primary caregiver is designated; ideally, someone who does not have an underlying condition that places them at increased risk of severe influenza disease. Although no studies have assessed the use of masks at home to decrease the spread of infection, using a surgical or procedure mask by the patient or caregiver during interactions may be beneficial. Separation of eating utensils for use by a patient with influenza is not necessary, as long as they are washed with warm water and soap. Additional information on measures to limit the spread of pandemic influenza in the home and community can be found in **Supplement 4** and **Supplement 8**.

TABLE 1. PANDEMIC INFLUENZA INFECTION CONTROL GUIDANCE FOR HEALTHCARE PROVIDERS

COMPONENT	RECOMMENDATIONS
STANDARD PRECAUTIONS	See www.cdc.gov/ncidod/hip/ISOLAT/std_prec_excerpt.htm
Hand hygiene	Perform hand hygiene after touching blood, body fluids, secretions, excretions, and contaminated items; after removing gloves; between patient contacts. Hand hygiene includes both handwashing with either plain or antimicrobial soap and water and use of alcohol-based products (gels, rinses, foams) that contain an emollient and do not require the use of water. If hands are visibly soiled or contaminated with respiratory secretions, they should be washed with soap (either non-antimicrobial or antimicrobial) and water. In the absence of visible soiling of hands, approved alcohol-based products for hand disinfection are preferred over antimicrobial or plain soap and water because of their superior microbiocidal activity, reduced drying of the skin, and convenience.
Personal protective equipment (PPE) • Gloves • Gown • Face/eye protection (e.g., surgical or procedure mask and goggles or a face shield)	• For touching blood, body fluids, secretions, excretions, and contaminated items; for touching mucous membranes and nonintact skin • During procedures and patient-care activities when contact of clothing/exposed skin with blood/body fluids, secretions, and excretions is anticipated • During procedures and patient care activities likely to generate splash or spray of blood, body fluids, secretions, excretions
Safe work practices	Avoid touching eyes, nose, mouth, or exposed skin with contaminated hands (gloved or ungloved); avoid touching surfaces with contaminated gloves and other PPE that are not directly related to patient care (e.g., door knobs, keys, light switches).
Patient resuscitation	Avoid unnecessary mouth-to-mouth contact; use mouthpiece, resuscitation bag, other ventilation devices to prevent contact with mouth and oral secretions.
Soiled patient care equipment	Handle in a manner that prevents transfer of microorganisms to oneself, others and to environmental surfaces; wear gloves if visibly contaminated; perform hand hygiene after handling equipment.
Soiled linen and laundry	Handle in a manner that prevents transfer of microorganisms to oneself, others, and to environmental surfaces; wear gloves (gown if necessary) when handling and transporting soiled linen and laundry and perform hand hygiene
Needles and other sharps	Use devices with safety features when available; do not recap, bend break or hand-manipulate used needles; if recapping is necessary, use a one-handed scoop technique; place used sharps in a puncture-resistant container.

TABLE 1. PANDEMIC INFLUENZA INFECTION CONTROL GUIDANCE FOR HEALTHCARE PROVIDERS (CONT.)

COMPONENT	RECOMMENDATIONS
STANDARD PRECAUTIONS (cont.)	
Environmental cleaning and disinfection	Use EPA-registered hospital detergent-disinfectant; follow standard facility procedures for cleaning and disinfection of environmental surfaces; emphasize cleaning/disinfection of frequently touched surfaces (e.g., bed rails, phones, lavatory surfaces).
Disposal of solid waste	Contain and dispose of solid waste (medical and non-medical) in accordance with facility procedures and/or local or state regulations; wear gloves when handling waste; wear gloves when handling waste containers and perform hand hygiene
Respiratory hygiene/cough etiquette Source control measures for persons with symptoms of a respiratory infection; implement at first point of encounter (e.g., triage/reception areas) within a healthcare setting.	Have the patient cover the mouth/nose when sneezing/coughing; use tissues and dispose in no-touch receptacle; perform hand hygiene after contact with respiratory secretions; wear a mask (procedure or surgical) if tolerated; sit or stand as far away as possible (more than 3 feet) away from persons who are not ill.
DROPLET PRECAUTIONS	www.cdc.gov/ncidod/hip/ISOLAT/droplet_prec_excerpt.htm
Patient placement	Place patients with influenza in a private room or cohort with other patients with influenza.* Keep door closed or slightly ajar; maintain room assignments of patients in nursing homes and other residential settings, and apply droplet precautions to all persons in the room. *During the early stages of a pandemic, infection with influenza should be laboratory-confirmed, if possible.
Personal protective equipment	Wear a surgical or procedure mask for entry into patient room; wear other PPE as recommended for standard precautions.
Patient transport	Limit patient movement outside of room to medically necessary purposes; have patient wear a procedure or surgical mask when outside the room.
Other	Follow standard precautions and facility procedures for handling linen and laundry and dishes and eating utensils, and for cleaning/disinfection of environmental surfaces and patient care equipment, disposal of solid waste, and postmortem care.

TABLE 1. PANDEMIC INFLUENZA INFECTION CONTROL GUIDANCE FOR HEALTHCARE PROVIDERS (CONT.)

COMPONENT	
AEROSOL-GENERATING PROCEDURES	During procedures that may generate small particles of respiratory secretions (e.g., endotracheal intubation, bronchoscopy, nebulizer treatment, suctioning), healthcare personnel should wear gloves, gown, face/eye protection, and a fit-tested N-95 respirator or other appropriate particulate respirator.

Standard Precautions for home health care

Healthcare providers who enter homes where there is a person with an influenza-like illness should follow the recommendations for Standard and Droplet Precautions. Standard Precautions include performing hand hygiene and respiratory hygiene/cough etiquette, wearing gloves and gowns, using face/eye protection when needed; and following safe work practices.

Droplet Precautions for home health care

Healthcare providers who enter homes where there is a person with an influenza-like illness should follow the recommendations for Standard and Droplet Precautions. Droplet Precautions include all Standard Precautions plus separating the patient from others in the household as much as possible and wearing a surgical or procedure mask for patient interactions. Professional judgment should be used in determining whether to don a mask upon entry into the home or only on entering the patient's room. Factors to consider in this decision include the possibility that others in the household may be infectious and the extent to which the patient is ambulating within the home.

APPENDIX 1. CLINICAL PRESENTATION AND COMPLICATIONS OF SEASONAL INFLUENZA

Although often quite characteristic, the clinical picture of seasonal influenza can be indistinguishable from illness caused by other respiratory infections. The frequent use of non-specific terms such as "flu" and "influenza-like illness" makes the clinical diagnosis of influenza even more indefinite. Even when the diagnosis of influenza is confirmed, management can be challenging, as influenza virus infection can result in subclinical infection, mild illness, uncomplicated influenza, or exacerbation of underlying chronic conditions to fulminant deterioration, and can result in a wide variety of complications.

This appendix provides a brief description of the common presentations and complications of seasonal human influenza. Novel and pandemic influenza viruses might, however, cause quite different clinical syndromes than seasonal influenza. For instance, seasonal influenza-related complications more commonly affect those at the extremes of age, whereas previous pandemics resulted in disproportionate morbidity and mortality in young and previously healthy adults. It will be essential to describe and disseminate the clinical features of novel or pandemic influenza cases as soon as they are identified. Appendix 2 includes a brief clinical summary of illnesses associated with previous influenza pandemics and with avian influenza A (H5N1) virus in humans.

Presentation

- A typical case of uncomplicated seasonal influenza begins abruptly and is manifested by systemic symptoms such as fever, chills, myalgias, anorexia, headache, and extreme fatigue. Fever typically lasts 2–3 days and usually reaches 38–40°C, but can be higher (particularly in children).
- Respiratory tract symptoms such as nonproductive cough, sore throat, and upper respiratory congestion occur at the same time, although these may be overshadowed by systemic complaints.
- Physical examination typically reveals fever, weakness, mild inflammation of the upper respiratory tract, and rare crackles on lung examination, but none of these findings is specific for influenza.
- In uncomplicated illness, major symptoms typically resolve after a limited number of days, but cough, weakness, and malaise can persist for up to 2 weeks.
- In the elderly and in infants, the presenting signs can include respiratory symptoms with or without fever, fever only, anorexia only, lassitude, or altered mental status. In children, fevers are often higher than in adults and can lead to febrile seizures. Gastrointestinal manifestations (e.g., vomiting, abdominal pain, diarrhea) occur more frequently in children. Fever or apnea without other respiratory symptoms might be the only manifestations in young children, particularly in neonates.

Influenza is difficult to distinguish from illnesses caused by other respiratory pathogens on the basis of symptoms alone. Fever and cough, particularly in combination, are modestly predictive of influenza in unvaccinated adults, as is the combination of fever, cough, headache, and pharyngitis in children. Other constitutional signs and symptoms, such as chills, rigors, diaphoresis, and myalgias, are also suggestive. The positive predictive value of any clinical definition is strongly dependent on the level of influenza activity and the presence of other respiratory pathogens in the community.

Routine laboratory findings

No routine laboratory test results are specific for influenza. Leukocyte counts are variable, although thrombocytopenia and severe leukopenia have been described in fulminant cases. Leukocytosis of >15,000 cells/ml should raise suspicion for a secondary bacterial process. Comprehensive laboratory testing might reveal other influenza-related complications (see below).

Differential diagnosis

The fever and respiratory manifestations of seasonal influenza are not specific and can occur with several other pathogens, including respiratory syncytial virus (RSV), parainfluenza viruses, adenoviruses, human metapneumovirus, rhinoviruses, coronaviruses, and *Mycoplasma pneumoniae*. In contrast to influenza viruses, most of these pathogens do not usually cause severe disease, particularly in previously healthy adults. RSV and parainfluenza viruses can, however, lead to severe respiratory illness in young children and the elderly and should be considered in the differential diagnosis if circulating in the community. Even if an alternate etiology is determined, viral or bacterial co-infections can still be a possibility.

The tendency for influenza to occur in community epidemics and to affect persons of all ages can sometimes allow the clinician to diagnose seasonal influenza with reasonable certainty in the absence of laboratory testing. Nevertheless, a definitive diagnosis requires laboratory testing. Rapid influenza diagnostic tests and immunofluorescence testing using a panel of respiratory pathogens have become increasingly available for aiding clinical management of patients with suspected influenza. Further information on diagnostic testing for influenza can be found at http://www.cdc.gov/flu/professionals/labdiagnosis.htm.

Complications

Groups at risk for complications of influenza

The following groups are currently recognized by the Advisory Committee on Immunization Practices (ACIP) to be at higher risk for complications of seasonal influenza (e.g., hospitalization; death) compared to healthy older children and younger adults:[4]

- Persons aged ≥65 years
- Residents of nursing homes and other chronic-care facilities that house persons of any age who have chronic medical conditions
- Adults and children who have chronic disorders of the pulmonary or cardiovascular systems, including asthma
- Adults and children who required regular medical follow-up or hospitalization during the previous year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression (including immunosuppression caused by medications or by infection with human immunodeficiency virus [HIV])
- Children and adolescents (aged 6 months–18 years) who are receiving long-term aspirin therapy (and are therefore at risk for Reye syndrome)
- Pregnant women
- All children aged <2 years
- All persons with conditions that can compromise respiratory function or the handling of respiratory secretions, or that can increase the risk of aspiration

Excluding the last group, in 2003 approximately 85 million persons in the United States belonged to one or more of these target groups.

Types of influenza complications

Exacerbations of underlying chronic diseases are the most common serious complications of influenza. Complications are frequently related to underlying respiratory disease, such as chronic obstructive pulmonary disease (COPD). In some cases, typical influenza symptoms might be brief or minimal compared to the exacerbation of the underlying disease, particularly in the elderly.

[4] Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2005;54:1-40 www.cdc.gov/mmwr/pdf/rr/rr54e713.pdf.

Secondary bacterial pneumonia, another common complication, is characterized by an initial improvement in influenza symptoms over the first few days followed by a return of fever, along with a productive cough and pleuritic chest pain. Findings include lobar consolidation on chest x-ray and, in adults, sputum smears positive for leukocytes and bacteria. The most commonly isolated pathogens are *Streptococcus pneumoniae, Staphylococcus aureus,* group A *Streptococcus*, and *Haemophilus influenzae*.

Influenza virus infection can also result in a primary viral pneumonia. A prominent feature of previous influenza pandemics, primary influenza viral pneumonia is currently a relatively rare outcome of seasonal influenza in adults. In contrast, children with pneumonia are more likely to have a viral etiology, including influenza than a bacterial cause. Primary influenza pneumonia usually begins abruptly, with rapid progression to severe pulmonary disease within 1–4 days. Physical and radiologic findings are consistent with diffuse interstitial and/or alveolar disease, including bilateral inspiratory crackles on auscultation and diffuse pulmonary infiltrates on chest radiographs. Hypoxia and hemoptysis indicate a poor prognosis, and recovery can take up to 1–2 weeks. Mixed viral-bacterial pneumonia is slightly more common than primary viral pneumonia, and, although mixed pneumonia may have a slower progression, the two are often indistinguishable. Bacterial pathogens in mixed infections are similar to those found in secondary bacterial pneumonias.

Bronchiolitis due to influenza is more common in children, with a clinical picture similar to that of RSV or parainfluenza virus infections. Influenza is a cause of croup (laryngotracheobronchitis) in children, and, although influenza viruses are a less common etiology than other respiratory viruses, the illness can be more severe. Children with influenza can also develop otitis media, due to either direct viral infection or secondary bacterial involvement. Similarly, bacterial sinusitis can develop in older children and adults with influenza.

Seasonal influenza can cause a range of cardiovascular complications, most commonly as an exacerbation of an underlying condition such as congestive heart failure. Pregnant women and children with congenital heart defects can also experience worsening cardiac function during an influenza illness. Cardiac inflammation, such as myocarditis and pericarditis, can be found occasionally, although clinical manifestations are rare. Available reports suggest that myocarditis might have occurred more frequently during pandemic years. Influenza virus is not typically identified in heart tissue, suggesting that the host inflammatory response might play a role. Although influenza has been associated in rare instances with sudden death possibly due to cardiac arrhythmia, this outcome has been difficult to investigate.

Gastrointestinal involvement is uncommon with seasonal influenza, although more commonly reported in children. Manifestations can include vomiting and diarrhea, sometimes leading to significant dehydration. Transient hepatic inflammation can occur in rare circumstances.

Myositis related to influenza is another complication more commonly found in children, although more frequently associated with influenza B. Involvement may be limited to pain and weakness of the lower extremities but can progress to rhabdomyolysis and renal failure in some cases.

Among the neurologic complications associated with seasonal influenza, uncomplicated self-limited febrile seizures are the most common, usually occurring in younger children with high fever. Influenza-associated encephalopathy, characterized by an acute alteration in mental status within the first few days of fever onset, is a recently recognized complication of influenza in children. Most reports of influenza-associated encephalopathy have been in Japanese children, but the condition has been reported sporadically in other countries, including the United States. The syndrome can include seizures, neurologic deficits, obtundation, and coma. While most children recover completely, some cases can result in permanent sequelae or death. This condition might be due to an abnormal host inflammatory response without viral infection of the central nervous system. Guillain-Barre syndrome and transverse myelitis have been reported to occur in very rare instances after influenza, but no definite etiologic relationship has been established.

Reye syndrome is another serious neurologic complication associated with influenza. It is characterized by an acute encephalopathy combined with hepatic failure in the absence of inflammation in either the brain or the liver. Hepatic

involvement includes fatty infiltration, hypoglycemia, and hyperammonemia, whereas neurologic manifestations include cerebral edema, delirium, coma, and respiratory arrest. Reye syndrome was found to be associated with the use of aspirin in children; its incidence has decreased dramatically since the 1980s after aspirin use was discouraged in children.

Seasonal influenza can be associated with systemic complications, such as sepsis and shock. Sepsis caused by invasive co-infection with *Staphylococcus aureus*, including methicillin-resistant *S. aureus* (MRSA), or other bacteria, such as *Neisseria meningitidis* has been reported. Toxic shock syndrome without bacterial co-infection has also been reported.

APPENDIX 2. CLINICAL PRESENTATION AND COMPLICATIONS OF ILLNESSES ASSOCIATED WITH AVIAN INFLUENZA A (H5N1) AND PREVIOUS PANDEMIC INFLUENZA VIRUSES

Human infections with different avian influenza A viruses have emerged and caused mild to severe illness in recent years, including H9N2, H7N7, H7N3, and H7N2. One novel subtype, influenza A (H5N1), has repeatedly caused limited outbreaks of severe and fatal human disease in recent years and therefore has been of particular concern.

Human infection with avian influenza A (H5N1)

The H5N1 subtype first came to widespread public attention in 1997, when a poultry outbreak of highly pathogenic avian influenza A (H5N1) in Hong Kong caused illness in 18 humans. These cases were the first identified instances of direct avian-to-human transmission of an avian influenza A virus that led to severe disease. Clinical features ranged from asymptomatic infection or mild upper respiratory symptoms to severe pneumonia and death. Most cases presented with fever, headache, malaise, myalgia, sore throat, cough, and rhinorrhea; a few persons also had conjunctivitis or gastrointestinal distress. Seven persons, mostly children, developed only mild upper respiratory infections, whereas 11 developed severe primary viral pneumonia with rapid deterioration. Most patients in this latter group developed lymphopenia; six developed acute respiratory distress syndrome (ARDS), and five developed multi-organ system failure. Other abnormalities included pulmonary hemorrhage, renal dysfunction, liver failure, pancytopenia, hemophagocytosis, and Reye syndrome (with aspirin ingestion). Notably, none of the patients had secondary bacterial pneumonia. Six of the 18 infected persons eventually died.

Avian influenza A (H5N1) resurfaced in Hong Kong in February 2003, in a father and son returning from Fujian Province, China. Both presented with influenza-like symptoms, chest radiograph abnormalities, and lymphopenia. The father's status rapidly deteriorated, and he developed severe lung involvement and hemophagocytosis; the 8-year-old son recovered. Of note, the father's 7-year-old daughter had also died of a pneumonia-like illness while in China, but the cause of her illness was not determined. The boy reported close contact with live chickens during his visit to China, but no definite source for H5N1 was found.

The most recent human outbreak of avian influenza A (H5N1) has been ongoing since December 2003. This outbreak has been associated with an extensive H5N1 epizootic among poultry in Asia. Transmission continues to be predominantly from birds to humans, although a few instances of limited human-to-human transmission have been suspected.

Reports published from Vietnam and Thailand describe the early confirmed H5N1 cases from this outbreak. These reports characterize human illness with avian influenza A (H5N1) virus infection as a primarily respiratory febrile illness that progresses to severe disease in a high proportion of cases. Among 10 Vietnamese patients,[5] all were previously healthy children or young adults (mean age, 13.7 years) who presented to medical attention with fever, cough, and dyspnea. None of the patients had other respiratory symptoms, such as sore throat or rhinorrhea, but seven developed diarrhea. Significant lymphopenia was observed in all 10 cases, and moderate thrombocytopenia occurred. All 10 had marked abnormalities on chest radiograph, and eight patients—all of whom eventually died—required mechanical ventilation for respiratory failure. Respiratory cultures suggested bacterial pneumonia in two patients.

Of 12 cases described from Thailand,[6] seven were aged <14 years, and all but one were previously healthy. All of the patients developed fever, cough, and dyspnea, and six patients were reported with myalgia and diarrhea. Decreased leukocyte counts were reported in seven cases, thrombocytopenia occurred in four cases, and increased serum liver enzymes were found in eight.

[5] Tran TH, Nguyen TL, Nguyen TD, Luong TS, Pham PM, Nguyen VC, et al. Avian influenza A (H5N1) in 10 patients in Vietnam. N Engl J Med. 2004;350:1179-88.

[6] Chotpitayasunondh T, Ungchusak K, Hanshaoworakul W, Chunsuthiwat S, Sawanpanyalert P, Kijphati R, et al. Human disease from influenza A (H5N1), Thailand, 2004. Emerg Infect Dis. 2005;11:201-9.

All patients had negative blood cultures. They all had abnormal chest radiographs; nine developed respiratory failure with ARDS, whereas five developed cardiac failure, four had renal failure, and eight ultimately died. In the Vietnamese and Thai cases, respiratory deterioration occurred a median of 5 days after symptom onset, but the range was quite wide.

Whereas all patients described above presented with pulmonary symptoms, subsequently published case reports suggest that other clinical syndromes can occur with H5N1 infection.[7,8,9] In one report, a 39-year-old female with confirmed H5N1 from Thailand was initially admitted with symptoms of fever, vomiting, and diarrhea, and was found to have significant lymphopenia. She developed shortness of breath approximately 12 days after illness onset and soon progressed to ARDS and death. A 4-year-old male from Vietnam presented for medical attention with severe diarrhea, developed acute encephalitis with coma, and died soon thereafter. Although avian influenza A (H5N1) was later detected in throat, stool, serum, and cerebrospinal fluid specimens, the patient had no respiratory symptoms at presentation. This patient's 9-year-old sister died of a similar illness a few days before his illness began, but no H5N1 testing was performed. Asymptomatic H5N1 infection, detected by seroconversion, has been reported.

Updated information on avian influenza can be found at http://www.who.int/csr/disease/avian_influenza/en/.

Illnesses associated with previous pandemic viruses

Since most people do not have previous immunity to novel influenza A viruses, an influenza pandemic results in an increased rate of severe disease in a majority of age groups. Nevertheless, the three pandemics of the past century demonstrated significant variability in terms of morbidity. The 1918–19 pandemic was particularly notable in affecting young, healthy adults with severe illness. A significant proportion of patients developed fulminant disease, accompanied by a striking perioral cyanosis, leading to death within a few days. Postmortem examinations in these patients frequently revealed denuding tracheobronchitis, pulmonary hemorrhage, or pulmonary edema. Others survived the initial illness, only to die of a secondary bacterial pneumonia, usually due to *Streptococcus pneumoniae*, *Staphylococcus aureus*, group A *Streptococcus*, or *Haemophilus influenzae*.

The clinical features of the subsequent pandemics of 1957–58 and 1968–69 were also typical of influenza-like illness, including fever, chills, headache, sore throat, malaise, cough, and coryza, but were milder compared to the 1918–19 pandemic. On a population level, the impact of influenza in 1957–58 was only one-tenth that observed in 1918–19, and the excess death rate in 1968–69 was only half that observed during 1957–58. However, death rates were elevated among the chronically ill and the elderly, and the occurrence of severe complications, such as primary viral pneumonia, was notably increased in healthy young adults during the 1957–58 pandemic, particularly in pregnant women.

Implications for the next pandemic

The characteristic clinical features of the next influenza pandemic cannot be predicted. It is reasonable to assume that most affected persons will have the typical features of influenza (e.g., fever, respiratory symptoms, myalgia, malaise). However, past pandemics have varied considerably with regard to severity and associated complications. Illnesses caused by novel influenza viruses such as avian influenza A (H5N1) might predict the potential characteristics of pandemic influenza, but H5N1 has not adapted to spread easily among humans, and its presentation and severity might change as the virus evolves. Even as the next pandemic begins and spreads, the characteristic features might change, particularly if successive waves occur over several months. Given this potential for a dynamic clinical picture, it will be important for clinicians and public health partners to work together to disseminate updated and authoritative information to the healthcare community on a regular basis.

[7] de Jong MD, Bach VC, Phan TQ, Vo MH, Tran TT, Nguyen BH, et al. Fatal avian influenza A (H5N1) in a child presenting with diarrhea followed by coma. N Engl J Med. 2005;352:686-91.

[8] Apisarnthanarak A, Kitphati R, Thongphubeth K, Patoomanunt P, Anthanont P, Auwanit W, et al. Atypical avian influenza (H5N1). Emerg Infect Dis 2004;10:1321-4.

[9] Beigel JH, Farrar J, Hayden FG, Hyer R, de Jong MD, Lochindrat S, et al. Avian influenza A (H5N1) infection in humans. N Eng J Med. 2005 Sep 29;353(13):1374-85.

APPENDIX 3. GUIDELINES FOR MANAGEMENT OF COMMUNITY-ACQUIRED PNEUMONIA, INCLUDING POST-INFLUENZA COMMUNITY-ACQUIRED PNEUMONIA

Rationale

Post-influenza bacterial community-acquired pneumonia will likely be a common complication during the next pandemic and might affect approximately 10% of persons with pandemic influenza, based on data from previous influenza pandemics. Assuming that pandemic influenza will affect about 15%–35% of the U.S. population, approximately 4.4 to 10.2 million cases of post-influenza bacterial community-acquired pneumonia could occur.

Post-influenza bacterial community-acquired pneumonia often presents as a return of fever, along with a productive cough and pleuritic chest pain, after an initial improvement in influenza symptoms over the first few days. Findings include lobar consolidation on chest x-ray and, in adults, sputum smear positive for leukocytes and bacteria. As with other bacterial infections, leukocytosis with increased immature forms may be present, but this finding is neither sensitive nor specific. The most common etiologies of post-influenza bacterial pneumonia are *Streptococcus pneumoniae, Staphylococcus aureus*, group A *Streptococcus*, and *Haemophilus influenzae*. Primary viral pneumonia, with abrupt onset and rapid progression, is more common than bacterial pneumonia in children, yet rare in adults. Physical and radiologic findings in viral pneumonia are consistent with interstitial and/or alveolar disease and include bilateral inspiratory crackles and diffuse infiltrates. Mixed viral-bacterial pneumonia is slightly more common than primary viral pneumonia, but they are often indistinguishable. Bacterial pathogens in mixed infections are similar to those found in secondary bacterial pneumonias. Droplet and Standard Precautions are currently recommended for community-acquired pneumonia of bacterial etiology.[9]

Treatment of community-acquired pneumonia, including post-influenza bacterial community-acquired pneumonia will pose challenges for clinicians during a pandemic. Secondary bacterial pneumonia following influenza virus infection will be difficult to distinguish from community-acquired pneumonia that is not preceded by influenza. Current guidelines for the treatment of adult community-acquired pneumonia (CAP) during the Interpandemic Period de-emphasize the use of diagnostic testing for pathogen-directed treatment and favor empiric therapy with safe and effective broad-spectrum antibacterials, especially extended-spectrum macrolides and fluoroquinolones. However, these antibacterials will likely be in short supply during a pandemic.

The guidelines in this appendix are therefore designed to assist clinicians in managing patients with community-acquired pneumonia, including post-influenza bacterial community-acquired pneumonia, in a setting of high patient volume and limited clinical resources, where the pressure to treat empirically will likely be even greater than during the Interpandemic Period. For adults, the guidance draws heavily from the current draft guidelines for the management of CAP developed jointly by the Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS).[10,11] For children, the guidance incorporates recommendations from the British Thoracic Society (BTS),[12] a published review,[13] and expert opinion.

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[9] Centers for Disease Control and Prevention. Guidelines for preventing health-care-associated pneumonia, 2003 recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee. Respir Care. 2004;49(8):926-39.

[10] Mandell LA, Bartlett JG, Dowell SF, File TM Jr, Musher DM, Whitney C; Infectious Diseases Society of America. Update of practice guidelines for the management of community-acquired pneumonia in immunocompetent adults. Clin Infect Dis. 2003; 37(11):1405-33.

[11] Niederman MS, Mandell LA, Anzueto A, Bass JB, Broughton WA, Campbell GD, et al. American Thoracic Society. Guidelines for the management of adults with community-acquired pneumonia. Diagnosis, assessment of severity, antimicrobial therapy, and prevention. Am J Respir Crit Care Med. 2001;163(7):1730-54.

[12] British Thoracic Society Standards of Care Committee. British Thoracic Society guidelines for the management of community acquired pneumonia in childhood. Thorax. 2002;57(suppl 1):i1-24..

[13] McIntosh, K. Community-acquired pneumonia in children. N Engl J Med. 2002;346:429-37.

Prevention

Efforts to maximize vaccination coverage against *Streptococcus pneumoniae* is an important component of post-influenza bacterial community-acquired pneumonia prevention during the Interpandemic, Pandemic Alert, and Pandemic Periods. Current guidelines on the use of the 23-valent pneumococcal polysaccharide vaccine among adults and the 7-valent pneumococcal conjugate vaccine among children are available.[14,15]

Site of care: inpatient versus outpatient

Adults

- IDSA-ATS draft guidelines recommend the use of severity scores, such as the Pneumonia PORT Severity Index (PSI) and the CURB-65 system,[16,17] to determine which patients can be safely treated as outpatients (Tables 2–5). The use of these or other similar systems could be extremely important during the next pandemic, as hospital beds will be in short supply. However, these systems should be used to supplement rather than replace the judgment of the individual clinician.

Children

- Current guidelines provide indicators for hospitalization of children with CAP. For infants, the indications include temperature >38.5 C, respiratory rate (RR) >70 breaths per minute, chest retractions (indrawing), nasal flaring, hypoxia, cyanosis, intermittent apnea, grunting, and poor feeding. Indications for hospitalization among older children include temperature >38.5 C, RR >50, chest retractions, nasal flaring, hypoxia, cyanosis, grunting, and signs of dehydration.

As with pandemic influenza, the decision to hospitalize for post-influenza bacterial community-acquired pneumonia during the Pandemic Period will rely on the physician's clinical assessment of the patient as well as availability of personnel and hospital resources. Although an unstable patient will be considered a high priority for admission, patients with certain high-risk conditions (see Appendix 1) might also warrant special attention. Home management with follow-up might be appropriate for well-appearing young children with fever alone.

[14] Prevention of pneumococcal disease among infants and young children: recommendations of the Advisory Committee on Immunization Practices. MMWR Morb Mortal Wkly Rep. 2000;49(RR-9).

[15] CDC. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep. 1997;46(RR-8).

[16] Fine MJ, Auble TE, Yealy DM, Hanusa BH, Weissfeld LA, Singer DE, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med.* 1997;336(4):243-50..

[17] Lim WS, van der Eerden MM, Laing R, Boersma WG, Karalus N, Town GI, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax. 2003;58(5):377-82.

TABLE 2. PNEUMONIA PORT SEVERITY INDEX (PSI) CALCULATION

Patient Characteristic	Points Assigned
Demographic Factor	
Age	
Male	Number of years
Female	Number of years–10
Nursing home resident	+10
Comorbid illnesses	
Neoplastic disease	+30
Liver disease	+20
Congestive heart failure	+10
Cerebrovascular disease	+10
Renal disease	+10
Physical examination finding	
Altered mental status	+20
Respiratory rate >30 breaths/minute	+20
Systolic blood pressure <90 mm Hg	+20
Temperature <35°C or >40°C	+15
Pulse >125 beats/minute	+10
Laboratory and /or radiographic finding	
Arterial pH <7.35	+30
Blood urea nitrogen >30 mg/dl	+20
Sodium <130mmol/l	+20
Glucose >250 mg/dl	+10
Hematocrit <30%	+10
Hypoxemia <90% by pulse oximetry OR <60mm Hg by arterial blood gas	+10
Pleural effusion on baseline radiograph	+10

TABLE 3. PNEUMONIA SEVERITY INDEX RISK CLASSIFICATION

PSI Risk Class	Characteristics and Points	Recommended Site of Care
I	Age >50 years + no comorbid conditions, normal range vital signs, normal mental status	Outpatient
II	<70	Outpatient
III	71–90	Outpatient / Brief inpatient
IV	91–130	Inpatient
V	>130	Inpatient

TABLE 4. CURB-65 SCORING SYSTEM

Characteristic	Points
Confusion[1]	+1
Urea >7mmol/l (20mg/dl)	+1
Respiratory rate >30 breaths per minute	+1
Blood pressure (Systolic <90 or diastolic <60 mm Hg)	+1
Age >65 years	+1

[1] Based on a specific mental test or disorientation to person, place, or time.

TABLE 5. RECOMMENDED SITE OF CARE BASED ON CURB-65 SYSTEM

Number of Points	Recommended Site of Care
0–1	Outpatient
2	Admit to medical ward
3–5	Admit to medical ward or ICU

Diagnostic testing

Adults

Generally, the etiologies associated with CAP during the Interpandemic Periods will continue to occur during a pandemic. Familiarity with the appropriate use of available diagnostic tests is therefore a key feature of clinical preparedness.

- Draft IDSA-ATS guidelines recommend obtaining appropriate specimens for etiologic diagnosis whenever such an etiology would alter clinical care. Given that the most common etiologies of post-influenza bacterial community-acquired pneumonia—*S. pneumoniae* and *S. aureus*, including community-acquired methicillin-resistant *S. aureus* (CA-MRSA)—are treated differently, diagnostic testing should be performed to the extent feasible to distinguish among these pathogens.
- For hospitalized patients, blood cultures, pneumococcal urine antigen testing, and pleural fluid aspiration with Gram stain and culture should be considered.
- Because the diagnostic utility of sputum Gram stain and culture is highly dependent on patient and technical conditions, these are considered optional for hospitalized but non-severe patients.
- For patients admitted to an ICU, aspiration and Gram stain and bacterial culture of endotracheal secretions might also be useful.

Children

Diagnostic studies for identifying bacterial pneumonia in young children are severely limited.

- Blood cultures should be obtained from all children suspected of having post-influenza bacterial community-acquired pneumonia.
- Sputum samples are rarely useful in children, but tracheal or pleural fluid aspirates—if available—should be submitted for Gram stain and bacterial culture.
- If pleural effusions are present, they should be aspirated and submitted for Gram stain and culture.
- When feasible, antibiotic susceptibility testing of any bacterial isolates is encouraged to direct treatment.

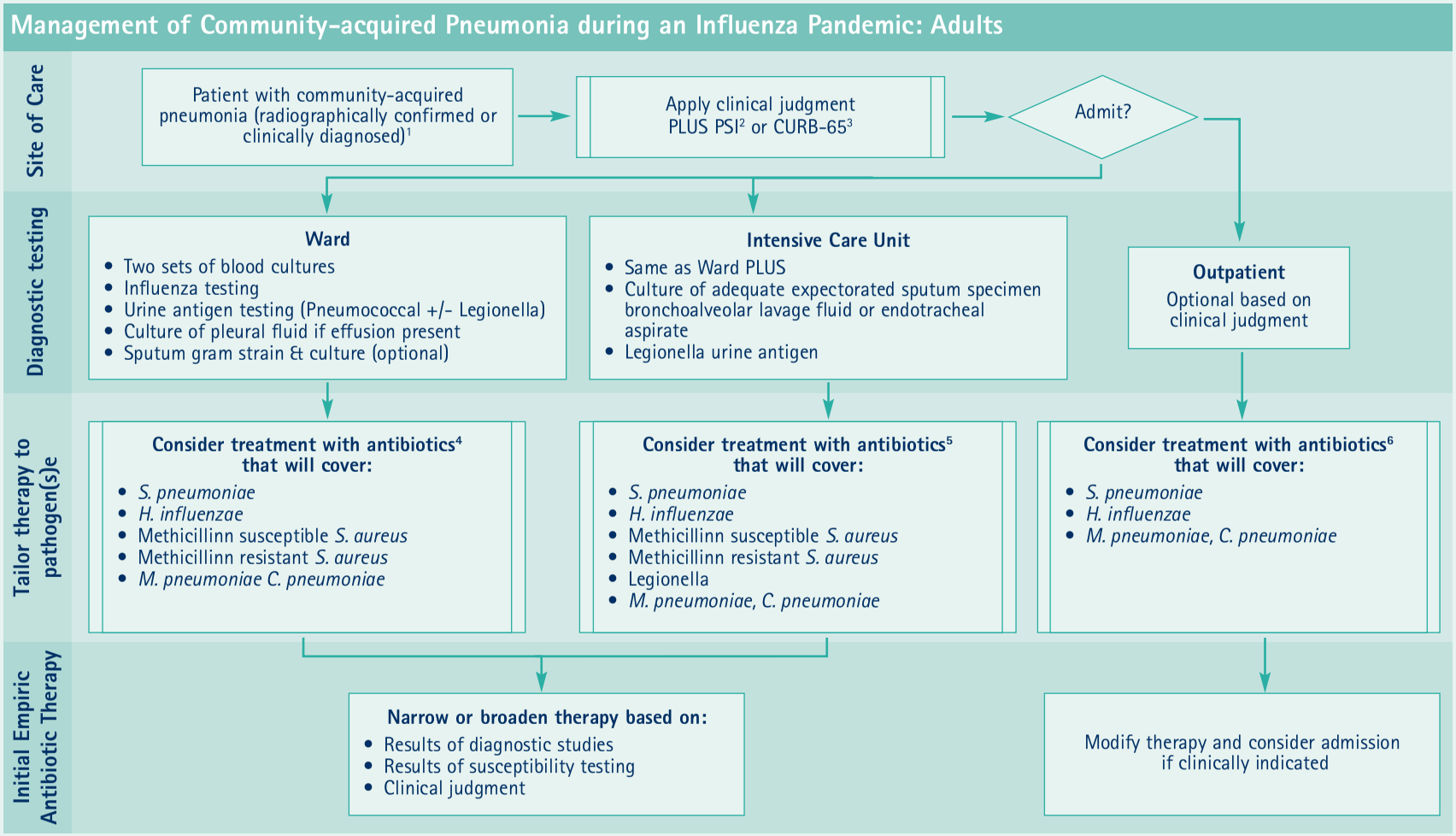
Antibiotic treatment

Adults and children

Antibiotics, particularly those needed to treat CAP, will likely be in short supply during the Pandemic Period. Therefore, use of empiric therapy for all persons with post-influenza bacterial community-acquired pneumonia will likely not be feasible. Antimicrobial therapy will have to be driven by culture and susceptibility testing of appropriate clinical specimens and by awareness of local antibiotic susceptibility patterns. (See Figures 1 and 2.)

- A history of preceding influenza-like illness, especially when pandemic influenza is circulating in the community, might help to screen patients.
- Empiric therapy in adults should be directed toward the most likely etiologies of post-influenza bacterial community-acquired pneumonia.
- Concurrent antiviral treatment might also be beneficial, depending on the timing and presentation of illness (see **Supplement 7**).

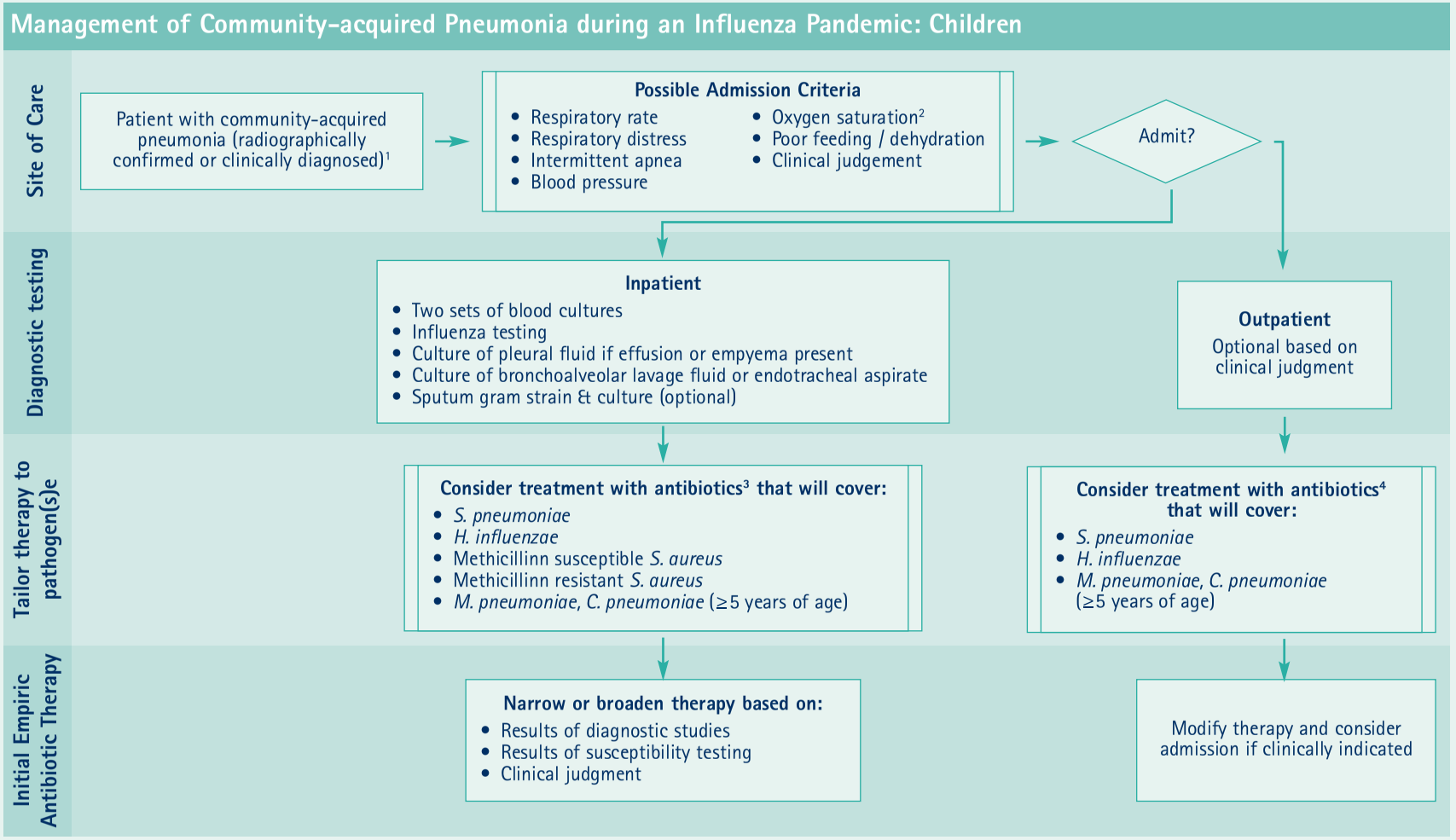
FIGURE 3. MANAGEMENT OF COMMUNITY-ACQUIRED PNEUMONIA DURING AN INFLUENZA PANDEMIC: ADULTS


Management of Community-acquired Pneumonia during an Influenza Pandemic: Adults
Site of Care
Patient with community-acquired pneumonia (radiographically confirmed or clinically diagnosed)[1]
Apply clinical judgment PLUS PSI[2] or CURB-65[3]
Admit?
Diagnostic testing
Ward
Two sets of blood cultures
Influenza testing
Urine antigen testing (Pneumococcal +/- Legionella)
Culture of pleural fluid if effusion present
Sputum gram strain & culture (optional)
Intensive Care Unit
Same as Ward PLUS
Culture of adequate expectorated sputum specimen bronchoalveolar lavage fluid or endotracheal aspirate
Legionella urine antigen
Outpatient
Optional based on clinical judgment
Tailor therapy to pathogen(s)e
Consider treatment with antibiotics[4] that will cover:
S. pneumoniae
H. influenzae
Methicillinn susceptible S. aureus
Methicillinn resistant S. aureus
M. pneumoniae C. pneumoniae
Consider treatment with antibiotics[5] that will cover:
S. pneumoniae
H. influenzae
Methicillinn susceptible S. aureus
Methicillinn resistant S. aureus
Legionella
M. pneumoniae, C. pneumoniae
Consider treatment with antibiotics[6] that will cover:
S. pneumoniae
H. influenzae
M. pneumoniae, C. pneumoniae
Initial Empiric Antibiotic Therapy
Narrow or broaden therapy based on:
Results of diagnostic studies
Results of susceptibility testing
Clinical judgment
Modify therapy and consider admission if clinically indicated

[1] Patients whose chest radiographs show no evidence of CAP should not be treated for CAP.
[2] Pneumonia Severity Index (Fine et al. NEJM 1997; 336: 243–50).
[3] Confusion, Uremia, Respiratory rate, Blood pressure, Age ≥65 (Lim et al. Thorax 2003; 58: 377–82).
[4] Possible antibiotic regimens for WARD INPATIENTS include
- ß-lactam PLUS macrolide PLUS either vancomycin or linezolid
- Fluoroquinolone PLUS either vancomycin or linezolid.

[5] Regimens for INTENSIVE CARE UNIT PATIENTS include those listed for WARD INPATIENTS but should include azithromycin or a fluoroquinolone.
[6] Possible oral antibiotic regimens for OUTPATIENTS include
- Previously healthy & no use of antimicrobials within the previous 3 months: macrolide or doxycycline.
- Comorbidities or use of antimicrobials within previous 3 months (choose from a different class): fluoroquinolone, telithromycin, ß-lactam PLUS a macrolide.
- In regions with a high rate of "high-level" macrolide-resistant S pneumoniae: fluoroquinolone telithromycin.

FIGURE 4. MANAGEMENT OF COMMUNITY-ACQUIRED PNEUMONIA DURING AN INFLUENZA PANDEMIC: CHILDREN


Management of Community-acquired Pneumonia during an Influenza Pandemic: Children
Site of Care
Patient with community-acquired pneumonia (radiographically confirmed or clinically diagnosed)[1]
Possible Admission Criteria
Respiratory rate
Respiratory distress
Intermittent apnea
Blood pressure
Oxygen saturation[2]
Poor feeding / dehydration
Clinical judgement
Admit?
Diagnostic testing
Inpatient
Two sets of blood cultures
Influenza testing
Culture of pleural fluid if effusion or empyema present
Culture of bronchoalveolar lavage fluid or endotracheal aspirate
Sputum gram strain & culture (optional)
Outpatient
Optional based on clinical judgment
Tailor therapy to pathogen(s)e
Consider treatment with antibiotics[3] that will cover:
S. pneumoniae
H. influenzae
Methicillinn susceptible S. aureus
Methicillinn resistant S. aureus
M. pneumoniae, C. pneumoniae (≥5 years of age)
Consider treatment with antibiotics[4] that will cover:
S. pneumoniae
H. influenzae
M. pneumoniae, C. pneumoniae (≥5 years of age)
Initial Empiric Antibiotic Therapy
Narrow or broaden therapy based on:
Results of diagnostic studies
Results of susceptibility testing
Clinical judgment
Modify therapy and consider admission if clinically indicated

[1] Although chest radiography is not necessary to make the diagnosis in all pediatric patients with CAP, patients who do undergo chest radiography and whose radiographs show no evidence of CAP should not be treated for CAP.

[2] Pulse oximetry should be performed for all children hospitalized with CAP.

[3] Possible antibiotic regimens for INPATIENTS include:
- Children <5 years of age: ß-lactam (e.g. Ampicillin, Amoxicillin, Amoxicillin/clavulanic acid, 3rd generation cephalosporin [cefotazime, ceftriazone]) PLUS either vancomycin or linezolid.
- Children ≥5 years of age: ß-lactam PLUS macrolide PLUS either vancomycin or linezolid.

[4] Possible oral antibiotic regimens for OUTPATIENTS include:
- Children <5 years of age: ß-lactam (e.g. Amoxicillin, Amoxicillin/clavulanic acid).
- Children ≥5 years of age: ß-lactam (e.g. Amoxicillin, Amoxicillin/clavulanic acid) or a macrolide depending on clinical severity. M. pneumoniae & C. pneumoniae generally present with less severe illness than S. pneumoniae or H. influenza.

supplement 6
vaccine distribution and use

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SUMMARY OF PUBLIC HEALTH ROLES AND RESPONSIBILITIES FOR VACCINE DISTRIBUTION AND USE

The roles and responsibilities of healthcare partners in vaccine distribution and use are described in **Supplement 3**.

INTERPANDEMIC AND PANDEMIC ALERT PERIODS

State and local health departments:

- Work with healthcare partners and other stakeholders to develop state-based plans for vaccine effectiveness, safety, distribution and use.

HHS agencies:

- Work with manufacturers to expedite public-sector vaccine purchasing contracts during a pandemic.
- Establish mechanisms for vaccine procurement and distribution.
- Develop guidance on priority groups for vaccination.
- Develop and stockpile vaccine for influenza strains with pandemic potential.
- Expedite the rapid development, licensure, and production of new influenza vaccines, as well as evaluate dose optimization strategies to maximize use of limited vaccine stocks.
- Estimate rates of reports of mild and severe adverse events following immunization (AEFIs) that may occur with mass influenza vaccination, and improve capacity for responding to them.
- Identify mechanisms and define protocols for conducting vaccine-effectiveness studies.
- Develop a system for monitoring state-specific vaccine coverage rates at regular intervals, using a pre-existing population-based survey.
- Develop reporting specifications for tracking data on vaccine administration and provide a vaccine database for optional use by states.
- Develop and distribute communication and education materials for use by states and other stakeholders.

PANDEMIC PERIOD

After the first reports of pandemic influenza are confirmed and before a pandemic vaccine becomes available

State and local health departments:

- If stockpiled vaccine of the pandemic subtype is available, work with healthcare partners and other stakeholders to distribute, deliver, and administer vaccines to designated groups.
- Mobilize healthcare partners, and prepare to activate state-based plans for distributing and administering vaccines.
- Keep the healthcare and public health workforce up-to-date on projected timelines for availability of vaccines against pandemic influenza.
- Review modifications, if any, to recommendations on vaccinating priority groups.
- Accelerate training in vaccination and vaccine monitoring for public health staff and for partners responsible for vaccinating priority groups.

PANDEMIC PERIOD (CONT.)

- Work with other governmental agencies and non-governmental organizations to ensure effective public health communications.

HHS agencies:

- Facilitate vaccine procurement, distribution, and tracking, working with private partners.
- Revise recommendations on vaccination of priority groups, guided by epidemiologic information about the pandemic virus (e.g., virulence, transmissibility, drug resistance, geographic spread, age-specific attack rates, morbidity and mortality rates).
- Provide state and local partners with guidance on reporting specifications for tracking administration of vaccine doses, to be used when vaccine becomes available.
- Provide state and local partners with guidance on Investigational New Drug (IND) and Emergency Use Authorization (EUA) procedures if new types of influenza vaccines for pandemic purposes are developed but not yet FDA approved.
- Provide guidance to state and local health departments on which adverse event reports are highest priority for investigation.
- Provide regulatory guidance to vaccine manufacturers for the manufacture and shipment of pandemic vaccines.

After a vaccine becomes available

State and local health departments:

- Work with healthcare partners and other stakeholders to distribute, deliver, and administer pandemic vaccines to priority groups.
- Monitor vaccine supplies, distribution, and use.
- Monitor and investigate adverse events.
- Phase-in vaccination of the rest of the population after priority groups have been vaccinated.
- Provide updated information to the public via the news media.
- Work with federal partners to evaluate vaccine-related response activities when the pandemic is over.

HHS agencies:

- Provide forecasts of pandemic vaccine availability from manufacturers.
- Continue to provide input into appropriate strain selection for seasonal influenza vaccine.
- Distribute public stocks of vaccines to state and large city health departments and to federal agencies with direct patient care responsibility, as needed.
- Implement protocols for assessing vaccine effectiveness.
- Monitor vaccine coverage rates.

S6-I. RATIONALE

The initial response to an influenza pandemic will include medical care, community containment and personal protective measures, and targeted use of antiviral drugs. Before a vaccine containing the circulating pandemic virus strain becomes available, pre-pandemic vaccine from stockpiles (if available for the pandemic subtype or partially cross-protective to the circulating virus) may be considered for persons in designated priority groups. Once a vaccine against the circulating pandemic virus strain becomes available, its distribution and delivery will be a major focus of pandemic response efforts.

Public health goals for vaccination during an influenza pandemic include:

- Developing pre-pandemic strategies for vaccine manufacturing and stockpiling that will maximize manufacturing capability
- Stockpiling influenza vaccine for strains and subtypes with pandemic potential
- Expediting development of a pandemic virus reference strain and distribution of the strain to vaccine manufacturers
- Accelerating production of a pandemic vaccine
- Maximizing the immune response to the vaccine
- Ensuring efficient and equitable distribution of pandemic vaccine, according to priority lists
- Rapidly determining vaccine effectiveness
- Providing ongoing and timely monitoring of vaccine coverage
- Providing ongoing and timely monitoring of vaccine safety

S6-II. OVERVIEW

Supplement 6 provides recommendations to state and local partners and other stakeholders on planning for the different elements of a pandemic vaccination program. The recommendations for the Interpandemic and Pandemic Alert Periods focus on planning for vaccine distribution, vaccination of priority groups, monitoring of adverse events, tracking of vaccine supply and administration, vaccine coverage and effectiveness studies, communications, legal preparedness, and training. The recommendations for the Pandemic Period focus on working with healthcare partners to implement plans for vaccination against pandemic influenza and initiate monitoring activities.

The activities described below are primarily the responsibility of government health authorities at the state, federal, local, and tribal levels. Additional issues that might be of interest to healthcare partners that administer vaccine are addressed in **Supplement 3**.

S6-III. RECOMMENDATIONS FOR THE INTERPANDEMIC AND PANDEMIC ALERT PERIODS

A. Vaccination against seasonal influenza virus strains

During the Interpandemic Period, state and local health departments should work with healthcare partners to enhance levels of 1) seasonal influenza vaccination in groups at risk for severe influenza and in healthcare workers, and 2) pneumococcal polysaccharide vaccination among those for whom it is recommended.

The success of the pandemic influenza vaccination program will be determined in large part by the strength of state and local vaccination programs during the Interpandemic Period. Higher annual vaccination rates will foster increased familiarity with

and public confidence in influenza vaccines, increased manufacturing capacity for influenza vaccines, and strengthened distribution channels. HHS is working with industry partners to ensure that influenza vaccine can be produced on an emergency basis at any time throughout the year (see Box 1).

Increased use of pneumococcal polysaccharide vaccine may decrease rates of secondary bacterial infections during a pandemic. Because large-scale pneumococcal vaccination might not be feasible once a pandemic occurs, the Interpandemic Period and Pandemic Alert is the ideal time to deliver this preventive measure. Pneumococcal vaccine is indicated for most persons for whom influenza vaccine is recommended. For specific guidelines on the prevention of pneumococcal disease, please see the Recommendations of the Advisory Committee on Immunization Practices (ACIP) (http://www.cdc.gov/mmwr/pdf/rr/rr4608.pdf).

B. Preparedness planning for vaccination against a pandemic influenza virus

A limited amount of avian influenza A (H5N1) vaccine is being stockpiled and will be considered for early use in the event of an H5N1 pandemic. Development of vaccines against other strains with pandemic potential is also being considered. A monovalent vaccine directed against the circulating pandemic virus strain of influenza should begin to be available within 4-6 months after identification of the new pandemic virus strain (Box 1). The number of persons who may be protected by vaccination depends on the manufacturing capacity, the amount of antigen per dose needed for a protective immune response, and the number of doses required. Although annual influenza vaccine is immunogenic in older children and adults with a single 15 microgram (µg) dose, a higher antigen concentration and/or two doses may be needed for pandemic vaccine where persons have no previous exposure to the influenza subtype and lack any immunity. Preliminary results from a recent clinical trial of an H5N1 vaccine in healthy adults suggested that two doses of 90 µg were required. Additional clinical trials are ongoing to evaluate possible ways to improve the immune response to lower the amounts of vaccine antigen needed for protection.

Initial pandemic vaccine stocks will be used to vaccinate designated priority groups (Part 1, Appendix D). After vaccination of these priority groups, vaccination of all those who desire it will be phased in depending on available supplies.

In working with healthcare partners to develop state-based plans for distributing vaccines, state and local health departments might use existing state-based plans for emergency mass distribution of medical supplies as the basis for developing local pandemic vaccination plans (e.g., smallpox and bioterrorism response plans).

1. Vaccination of priority groups

A list of priority groups for receiving vaccination and the rationale for prioritization is provided in Part 1, Appendix D, as interim recommendations. In addition, during a pandemic, changes may be made based on the characteristics of the causative virus (e.g., transmissibility, virulence, initial geographic distribution, age-specific attack rates, complication rates) and on vaccine effectiveness.

To prepare for vaccination of priority groups, state and local health departments should:

- Identify a process for reviewing national recommendations for pandemic influenza vaccination and developing state-specific modifications or refinements in priority groups, depending on local circumstances.
- Develop specific definitions for priority groups (e.g., public safety workers, essential service providers) identifying occupational categories and sub-categories, as needed, within each broad priority.
- Estimate the size of relevant priority groups.
- Develop a plan on how persons in priority groups would be identified at vaccination clinics and how vaccine would most efficiently be provided to those groups.
- Educate professional organizations and other stakeholders about the need for priority groups and the rationale for the groups currently recommended.

2. Vaccine production, procurement and distribution

HHS is working to expand pandemic influenza vaccine production capacity and will signal to manufacturers when to shift from annual to pandemic vaccine production and assure that pandemic vaccine is produced at full capacity.

At the onset of an influenza pandemic, HHS, in concert with the Congress in collaboration with the States, will work with the pharmaceutical industry to acquire vaccine directed against the pandemic strain. Distribution of pandemic vaccine to health departments and providers will occur via private-sector vaccine distributors or directly via manufacturer. (Only stockpiled pre-pandemic vaccine would be distributed by the federal government, if used.)

Each state and federal agency with direct patient care responsibility will receive available vaccine in proportion to the size of its population in defined priority groups. For priority groups that have been identified, state and local health departments should:

- Determine whether vaccine will be shipped directly from the manufacturer to vaccine providers or to public health clinics for further distribution
- Identify organizations that will provide vaccination to persons in priority groups (e.g., local health departments, occupational health clinics, private clinics identified by the employer or union of an occupational group)
- Identify contacts in and obtain written commitments from each clinic or facility responsible for vaccinating a priority group
- Work with these contacts to develop strategies for rapid distribution and administration of vaccines, taking into account vaccine security issues, cold chain requirements, and transport and storage issues
- Estimate the size of the priority groups that will be vaccinated based on extrapolation from national data or on local data, where available
- Identify locations for vaccination clinics that will be operated by health departments and enter into memoranda of agreement with organizations that agree to provide vaccinators or other staff
- Develop procedures for collecting, removing, and disposing of used syringes, needles, and other vaccination supplies
- Develop a plan for training vaccinators and other staff responsible for mass vaccination
- Develop strategies for vaccinating hard-to-reach populations

State and local health departments' plans should also specifically address the delivery of pandemic vaccine to medically underserved and migrant populations to improve equity in access within priority groups and, later, the general population.

If vaccinations are provided by private-sector organizations or providers at offices, clinics, or other sites, state and local health departments should:

- Develop mechanisms to allocate vaccine based on projected need.
- Develop mechanisms to collect unused vaccine (if any) from healthcare providers who have met their priority vaccination goals and distribute the vaccine to those who have not.
- Provide vaccination information to healthcare providers. This may best be accomplished by developing a communications plan for private-sector vaccine use.
- Monitor that vaccine administration follows existing plans on priority groups.

a) Second-dose vaccination

A vaccine against pandemic influenza will likely require two doses, administered at least a month apart, to provide a level of immunity comparable to that obtained with seasonal influenza vaccines. Recommendations on the number of required doses and the timing of the second dose will be issued once immunogenicity trials have been completed.

If two doses are required to achieve immunity, it will be necessary to ensure that vaccinated persons return for the second dose. State and local planners should do the following:

- Arrange for information about the need for a second dose to be provided at the time of vaccination.
- Ensure that planning for vaccine procurement and distribution to clinics and other facilities accounts for the need to use portions of future shipments for second doses, thus reducing the number of available first doses.
- Consider implementing a call-back system or immunization registry that would accomplish the goals of pandemic vaccination (see 3.b below).

b) Contingency planning for Investigational New Drug use

State and local health departments should be prepared to distribute unlicensed vaccines (if needed) under FDA's Investigational New Drug (IND) provisions. Unlicensed vaccines might be needed, for example, if pandemic spread is rapid and standard vaccine efficacy and safety tests are not completed in time to play a role in the response.

IND provisions require strict inventory control and record-keeping, completion of a signed consent form from each vaccinee, and mandatory reporting of specified types of adverse events. IND provisions also require approval from Institutional Review Boards (IRBs) in hospitals, health departments, and other vaccine-distribution venues. The FDA regulations permit the use of a national or "central" IRB. A treatment IND is one IND mechanism that FDA has available for use and is especially suited for large scale use of investigational products (http://www.access.gpo.gov/nara/cfr/waisidx_99/21cfr_99.html).

As an alternative to IND use of an unapproved antiviral drug, HHS may utilize the drug product under Emergency Use Authorization procedures as described in the FDA draft Guidance "Emergency Use Authorization of Medical Products" (http://www.fda.gov/cber/gdlns/emeruse.pdf).

3. Vaccine monitoring and data collection

To ensure optimal use of a new pandemic influenza vaccine, state and local health departments should be prepared to collect data on vaccine effectiveness, vaccine supply and distribution, vaccine coverage, and vaccine safety.

a) Vaccine effectiveness

Vaccine effectiveness will be assessed by comparing rates of influenza-related illness, hospitalization, and/or death among vaccinated and unvaccinated persons. These studies will be implemented by CDC in collaboration with healthcare and university partners and with state and local health departments that participate in influenza surveillance systems.

b) Vaccine supply and distribution

Mechanisms for tracking vaccine supply and distribution will depend on how vaccine is purchased and distributed. Tracking will be implemented by state and local health authorities-who will have major responsibility for allocation decisions-working in association with CDC and vaccine producers. Data also will be obtained from vaccine producers and commercial distributors.

- Vaccine tracking and coverage information may be used by federal, state, and local decision-makers to estimate adverse event rates based on the number of doses administered and to determine if vaccine is being administered according to established priority groups for pandemic vaccine (especially in the early phases of vaccination). Data will be collected from individual providers, collated at the local and state levels, and reported to federal authorities on a scheduled routine basis.

- States with immunization registries may adapt them for use in tracking coverage with pandemic influenza vaccine. Or, states may use a vaccine database that will be supplied by CDC. At a minimum, tracking data should include:
  - Number of doses administered, by date and age, priority group, and state or county (or zip code)
  - Number of doses that represent second doses, as applicable
- State and local authorities may consider additional data requirements for their own needs.

c) Vaccine coverage

CDC will work with states to develop a system for monitoring vaccination rates at regular intervals, using a pre-existing population-based survey tool (e.g., Behavioral Risk Factor Surveillance System) that provides national and state-level estimates and complements the vaccine tracking systems described above.

d) Vaccine safety

State and local health departments should develop a system to report and investigate adverse events following immunization (AEFI) with a pandemic influenza vaccine. Planning steps might include:

- Designating a state-level coordinator to plan for and implement adverse-events reporting and outreach to and education of providers (e.g., adapting and distributing federally developed Dear Doctor letters and materials for vaccine recipients) and who will serve as the state's contact with federal government staff overseeing the Vaccine Adverse Event and Reporting System (VAERS) (www.vaers.hhs.gov).
- Reviewing existing policies for AEFI reporting and follow-up to ensure timeliness of reporting.
- Developing a plan to ensure timely reporting of and communication about large numbers of AEFI reports.
- Reviewing procedures for and familiarizing program staff with the strengths, limitations, and objectives of VAERS. VAERS typically involves direct reporting by individual healthcare providers, with periodic feedback to the states. During a pandemic, some state health departments may wish to receive direct reports of AEFI to conduct investigations of adverse events and minimize duplicate reporting of adverse events to VAERS. State-level AEFI reporting can build on the infrastructure and experience developed during the 2003 smallpox vaccination program.

  Adverse events related to use of IND vaccines may be reported through other mechanisms in addition to or in place of VAERS, in accordance with specific regulatory or policy requirements. Adverse events will also be monitored through the Vaccine Safety Datalink (www.cdc.gov/nip/vacsafe/default.htm#VSD), a network of seven geographically diverse health maintenance organizations through which active surveillance vaccine safety studies are conducted. Another potential resource for vaccine safety research is CDC's Clinical Immunization Safety Assessment (CISA) network (www.vaccinesafety.org/CISA/index.htm).

4. Public health communications

The provision of vaccine information will be an important component of ongoing public health communication during a pandemic (see Supplement 10).

- State and local health departments should work with federal partners to disseminate accurate, useful, and consistent public health messages and should tailor information to local needs as indicated.
- Health departments should provide information to healthcare providers, state and local government officials, and the news media on:
  - Rationale for prioritization and list of priority groups (see Part 1, Appendix D)
  - Phasing of vaccination, if any, after priority groups have been vaccinated
  - When and where vaccination is available

- Importance of vaccination given likelihood of subsequent pandemic waves, particularly if public interest in vaccination has decreased

- As noted above, state and local health departments should be prepared to disseminate information on vaccine use to healthcare providers who purchase private stocks of pandemic influenza vaccine. In addition, all vaccine providers will need vaccine information sheets that describe the risks and benefits of, and contraindications to, vaccination.

5. Coordination with bordering jurisdictions

State and local health departments should review and coordinate vaccine distribution plans with health authorities in bordering jurisdictions, including neighboring states, tribal governments and other unique populations.

6. Legal preparedness

State and local health departments should ensure that appropriate legal authorities are in place to facilitate implementation of plans for distributing pandemic influenza vaccines. Health departments might undertake these legal preparedness steps:

- Ensure that plans for distribution of vaccines are reviewed by appropriate legal authorities.
- Determine whether state and local laws allow non-licensed volunteers or healthcare workers from other jurisdictions to administer influenza vaccines.
- Work with professional organizations and unions to consider options for emergency performance of tasks outside of standard job descriptions.
- Determine whether state and local laws allow mandatory vaccination to the protect public health, if needed.

7. Training

State and local health departments can assist healthcare partners in conducting training exercises to facilitate rapid and effective delivery and use of vaccines (see Supplement 3). Exercises and drills are essential to ensure that emergency procedures are in place and that roles and responsibilities are well understood. It may be useful, for example, to practice emergency implementation of mass vaccination (e.g., receiving large quantities of vaccine; storing and handling vaccine; setting up and staffing clinics; administering vaccine; testing information management systems; educating the public, media, and medical providers; targeting specific priority groups).

S6-IV. RECOMMENDATIONS FOR THE PANDEMIC PERIOD

A. Before a vaccine is available

Before a vaccine becomes available—state and local health departments should do the following:

- Meet with partners and stakeholders to review the major elements of the state's vaccine distribution plan.
- Modify the plan to account for possible updated interim recommendations on priority groups, projected vaccine supplies and timelines for availability, and staffing estimates for mass vaccination.
- Notify the medical community about the status of the plan and the expected availability of vaccines.
- If stockpiled vaccine of the pandemic subtype is available, work with healthcare partners and other stakeholders to distribute, deliver, and administer vaccines to designated groups.
- Update and disseminate public information on the production, distribution, and use of pandemic influenza vaccine before it becomes available (see **Supplement 10**).
- Conduct training for public health staff and partners involved in distributing and administering vaccines.

B. When a vaccine becomes available

- Once a vaccine is ready for distribution, state and local health departments should work with healthcare and community partners to activate plans to:
  - Vaccinate persons in priority groups, in accordance with existing recommendations.
  - Provide a second dose, if required for immunity.
  - Monitor vaccine supply, distribution, and use.
  - Monitor and investigate adverse events.
  - Continue communication with partners and the public.
- After priority groups have been vaccinated and additional vaccine stocks become available, public health authorities should phase-in vaccination of the rest of the population, based on age or other criteria that will ensure fair, equitable, and orderly distribution (see III.B). HHS will issue national recommendations to aid in this process.
- After the pandemic has ended, state and local health departments should evaluate all response activities, including vaccine tracking and delivery, adverse event monitoring, and communications.

BOX 1. DEVELOPMENT OF VACCINES AGAINST PANDEMIC STRAINS OF INFLUENZA

HHS is working with industry partners to ensure that influenza vaccine can be produced on an emergency basis at any time throughout the year (http://www.HHS.gov/nvpo/pandemicplan/) and to facilitate the development of cell- and recombinant-based interpandemic and pandemic influenza vaccines towards FDA licensure in U.S.-based manufacturing facilities. Activities in support of these goals include:

- Stimulating expanded manufacturing capacity by increasing annual demand for influenza vaccines by the CMS and CDC
- Securing a year-round egg supply for production of inactivated egg-based influenza vaccines
- Promoting the development of new technologies that:
  - Shorten the time required to develop a vaccine against a new strain of influenza.
  - Facilitate rapid expansion of vaccine production during a pandemic.
  - Optimize the use of limited vaccine supplies (e.g., antigen-sparing strategies).

HHS is also spearheading the development of human vaccines against avian influenza A (H5N1) and against other influenza A viruses with pandemic potential. HHS is providing funding to develop and manufacture pilot investigational lots of these vaccines at licensed influenza vaccine manufacturers and to evaluate their safety and immunogenicity in NIH-sponsored clinical trials in healthy adult, elderly, and pediatric populations.

HHS is acquiring commercial scale lots of influenza A (H5N1) vaccine to provide vaccine manufacturers with experience initially and then to establish and maintain stockpiles of pre-pandemic H5N1 vaccine.

APPENDIX. RESOURCES FOR MASS VACCINATION AGAINST PANDEMIC INFLUENZA

- **Department of Health and Human Services**
  - Guidelines for large-scale influenza vaccination clinic planning. Developed by CDC's National Immunization Program in response to the 2004 influenza vaccine shortage, this document was prepared to assist in planning for large vaccination clinics. It provides a general overview and guidelines for establishing and running a mass dispensing clinic (http://www.cdc.gov/flu/professionals/vaccination/pdf/vaxclinicplanning0405.pdf).
  - Guidelines for large-scale smallpox vaccination clinics. Although this document is specific to smallpox, most of the content is applicable to and can be adapted to other mass vaccination clinics (http://www.bt.cdc.gov/agent/smallpox/response-plan/files/annex-2.pdf).
  - Information on Investigational New Drug (IND) use and Emergency Use Authorization (EUA). Regulations governing IND applications are described in 21 CFR 312 (http://www.access.gpo.gov/nara/cfr/waisidx_99/21cfr312_99.html). Draft guidance for EUA is provided at http://www.fda.gov/cber/gdlns/emeruse.pdf.
- **Private-sector partners**
  - Community-based mass prophylaxis: a planning guide for public health preparedness. This report from Cornell University's Weill Medical College describes the five components of a mass prophylaxis/vaccination response to an epidemic (http://www.ahrq.gov/research/cbmprophyl/cbmpro.htm).

supplement 7
antiviral drug distribution and use

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SUMMARY OF PUBLIC HEALTH ROLES AND RESPONSIBILITIES FOR ANTIVIRAL DISTRIBUTION AND USE

INTERPANDEMIC AND PANDEMIC ALERT PERIODS

State and local health departments will work with healthcare partners to:

- Use antivirals in medical management of cases of novel strains of influenza
- Procure and maintain local stockpiles of antiviral drugs
- Develop state-based plans for distribution and use of antiviral drugs during a pandemic

HHS responsibilities:

- In advance of an influenza pandemic, HHS, in concert with the Congress and in collaboration with the States, will acquire sufficient quantities of antiviral drugs to treat 25% of the U.S. population and, in so doing, stimulate development of expanded domestic production capacity sufficient to accommodate subsequent needs through normal commercial transactions.
- Develop national guidance on use of antivirals during a pandemic, including identification of priority groups for antiviral drug treatment and prophylaxis.
- Continue procurement and maintenance of national supplies of antivirals in the Strategic National Stockpile.
- Maintain a program to test and extend dating of stockpiled antivirals, as needed, based on demonstration of continued potency.
- Develop protocols for monitoring antiviral effectiveness, safety, and resistance during a pandemic.
- Develop and distribute communication and education materials about antivirals for use by states and other stakeholders.

PANDEMIC PERIOD

State and local health departments will work with healthcare partners to:

- Prepare to activate state-based plans for distributing and administering antivirals to persons in priority groups.
- Review modifications, if any, to interim recommendations on antiviral prophylaxis in selected groups or circumstances.
- Accelerate training on appropriate use of antiviral drugs among public health staff and healthcare partners.
- Work with other governmental agencies and non-governmental organizations to ensure effective public health communications.

HHS responsibilities:

- Revise recommendations for treatment and prophylaxis with antivirals for priority groups, if necessary, guided by accumulating data about the pandemic virus (e.g., susceptibility, virulence, transmissibility, geographic spread, and age-specific attack rates).
- Provide state, territorial and local health departments, and healthcare partners with guidance on reporting specifications for tracking distribution, effectiveness, and safety of antivirals.

PANDEMIC PERIOD (CONT.)

- Work with WHO and global partners to determine the drug susceptibilities of the pandemic strain and monitor changes over time.
- Provide state, territorial and local health departments, and healthcare partners with guidance on reporting specifications for tracking distribution, effectiveness, and safety of antivirals.
- Provide information to health professionals and the public on issues related to availability and use of antiviral drugs during an influenza pandemic.

If pandemic influenza is detected in the United States:

State and local health departments will work with healthcare partners to:

- Distribute and deliver stockpiled supplies of antivirals, as appropriate, to healthcare facilities that will administer them to priority groups.
- Work with HHS to monitor antiviral drug use and effectiveness.
- Work with HHS to monitor and investigate adverse events.
- Provide updated information to the public via the news media.

Federal responsibilities:

- Establish and maintain stockpiles of influenza antiviral drugs at the SNS.
- Distribute antiviral drugs from the SNS to state and large city health departments and federal agencies with direct patient care responsibilities, as appropriate.
- Work with state and local health departments and healthcare partners to:
  - Evaluate the effectiveness of antivirals for treatment and prophylaxis.
  - Monitor the incidence of adverse events associated with antiviral use.
  - Monitor the emergence of antiviral resistance.
- Issue updated national guidelines for appropriate use of antivirals as the pandemic continues.
- Continue to provide information to health professionals and the public, as the situation changes, on drug availability, distribution, administration, side effects, and the rationale for targeted drug use.

S7-I. RATIONALE

Drugs with activity against influenza viruses ("antivirals") include the adamantanes *amantadine* and *rimantadine* and the neuraminidase inhibitors *oseltamivir* and *zanamivir* (see Table 1 and Appendix). Appropriate use of these agents during an influenza pandemic may reduce morbidity and mortality and diminish the overwhelming demands that will be placed on the healthcare system. Antivirals might also be used during the Pandemic Alert Period in limited attempts to contain small disease clusters and potentially slow the spread of novel influenza viruses. A huge and uncoordinated demand for antivirals early in a pandemic could rapidly deplete national and local supplies. Preparedness planning for optimal use of antiviral stocks is therefore essential.

S7-II. OVERVIEW

Supplement 7 provides recommendations to state and local partners on the distribution and use of antiviral drugs for treatment and prophylaxis during an influenza pandemic. The Interpandemic and Pandemic Alert Period recommendations focus on preparedness planning for the rapid distribution and use of antiviral drugs (e.g., procurement, distribution to priority groups, legal preparedness, training, and data collection on use, effectiveness, safety, and the development of drug resistance). These recommendations also cover the use of antiviral drugs in the management and containment of cases and clusters of infection with novel strains of influenza, including avian influenza A (H5N1) and human strains with pandemic potential.

The Pandemic Period recommendations focus on the local use of antiviral drugs in three situations: 1) when pandemic influenza is sporadically reported in the United States (without evidence of spread in the United States), 2) when there is limited transmission of pandemic influenza in the United States, and 3) when there is widespread transmission in the United States. National recommendations for optimal use of limited stocks of antivirals will be updated throughout the course of an influenza pandemic to reflect new epidemiologic and laboratory data. Interim recommendations will also be updated as an effective influenza vaccine becomes available.

The activities described below are primarily the responsibility of government health authorities at the state, federal, and local levels. Additional issues that may be of interest to healthcare partners who administer antiviral drugs are outlined in **Supplement 3**.

S7-III. RECOMMENDATIONS FOR THE INTERPANDEMIC AND PANDEMIC ALERT PERIODS

A. Use of antivirals in management of cases of novel influenza

Influenza infections may be due to:

1) Interpandemic (i.e., 'normal') seasonal strains of influenza[1]
2) Novel strains of influenza that do not appear to be easily transmissible but could be precursors to human pandemic strains (e.g., avian influenza A [H5N1] viruses)
3) Novel strains of influenza that demonstrate person-to-person transmission and therefore have pandemic potential (e.g., a new human pandemic strain)

In this document the term "novel strains of influenza" is used to refer to avian or animal influenza strains that can infect humans (like avian influenza A [H5N1]) and new or re-emergent human influenza viruses that cause cases or clusters of human disease. Criteria for early detection and identification of novel strains of influenza are discussed in **Supplement 1**.

1. Use of antivirals for treatment

A patient with a suspected case of avian influenza A (H5N1) or another novel strain of influenza should be isolated as described in **Supplement 4** and treated in accordance with the clinical algorithm for the Pandemic Alert Period provided in **Supplement 5**. As of fall 2005, the recommendation for treatment includes the use of oseltamivir or zanamivir, administered as early as possible and ideally within 48 hours after onset of symptoms. These neuraminidase inhibitors are preferred because the majority of avian influenza A (H5N1) viruses currently affecting humans are resistant to amantadine and rimantadine, and resistance to these drugs typically develops rapidly when they are used for treatment of influenza. Although resistance to

[1] Information on seasonal outbreaks of interpandemic influenza, including public health measures to contain outbreaks, can be found at http://www.cdc.gov/flu/.

zanamivir and oseltamivir can be induced in influenza A and B viruses *in vitro*, multiple passages in cell culture are usually required to produce neuraminidase inhibitor resistance, in contrast with adamantane resistance, which can develop after a single passage.[2,3] Because the neuraminidase inhibitors have different binding sites for the enzyme, cross-resistance between zanamivir- and oseltamivir-resistant viruses is variable. Current U.S. recommended doses for antiviral treatment are provided in Table 2.

2. Use of antivirals for prophylaxis of contacts

State and local health departments, in consultation with CDC, will consider whether it is necessary and feasible to trace a patient's close contacts and provide them with postexposure antiviral prophylaxis.

Close contacts may include family, schoolmates, workmates, healthcare providers, and fellow passengers if the patient has been traveling. If deemed necessary by public health authorities, these persons may receive post-exposure prophylaxis with oseltamivir, as zanamivir is not currently indicated for prophylaxis. If the exposure to the novel influenza virus strain occurs during the regular influenza season, the patient's healthcare contacts (who may also care for persons with seasonal influenza) should be vaccinated against seasonal influenza to reduce the possible risk of co-infection and reassortment of seasonal and novel strains.

3. Use of antivirals for containment of disease clusters

In special circumstances, state and local health departments could consider "targeted antiviral prophylaxis" as a community-based measure for containing small clusters of infection with novel strains of influenza (see **Supplement 8**). This measure could be implemented in small, well-defined settings such as the initial introduction of a virus with pandemic potential into a small community or a military base. However, once a pandemic is underway, such a strategy would not represent an efficient use of limited antiviral supplies.

Because targeted antiviral prophylaxis would require rapid delivery and administration of substantial stocks of antiviral drugs, its feasibility should be evaluated in light of antiviral drug supply and interim recommendations on antiviral drug use during a pandemic (see S7-III.B). Targeted antiviral prophylaxis would involve investigation of disease clusters, administration of antiviral treatment to persons with confirmed or suspected cases of pandemic influenza, and provision of drug prophylaxis to all persons in the affected community. Targeted antiviral prophylaxis would also require intensive case-finding in the affected area as well as effective communication with the affected community.

B. Preparedness planning for use of antivirals during a pandemic

1. National recommendations on use of antivirals during a pandemic

HHS is working with private-sector partners to increase production of antivirals and to procure additional stocks of antivirals for the Strategic National Stockpile (SNS) (http://www.HHS.gov/nvpo/pandemicplan/). Despite these efforts, demand for antivirals during an influenza pandemic is likely to far outstrip supplies available in stockpiles or through usual channels of distribution.

- A list of priority groups for receiving antiviral treatment or prophylaxis and the rationale for prioritization are provided in Part 1 Appendix D. During an actual pandemic, these recommendations could be modified, based on the characteristics of the causative virus (e.g., drug susceptibilities, initial geographic distribution, fatality rate, age-specific morbidity and mortality rates) and the effectiveness of implemented strategies.

2 McKimm-Breschkin JL. Resistance of influenza viruses to neuraminidase inhibitors — a review. Antiviral Res. 2000, 47:1-17.

[3] Tisdale M. Monitoring of viral susceptibility: new challenges with the development of influenza NA inhibitors. Rev Med Virol, 2000, 10:45-55.

2. State-level planning

State and local health departments should work with healthcare partners to develop state-based plans for antiviral need, procurement, distribution, and targeted use. Materials of potential benefit in these efforts include:

- Strategies outlined in Box 1 for optimizing antiviral use in treatment and prophylaxis. These strategies are based on scientific findings summarized in the July 2005 recommendations of the Advisory Committee on Immunization Practices (ACIP). http://www.cdc.gov/mmwr/PDF/rr/rr5408.pdf
- Clinical treatment algorithms provided in **Supplement 5**
- Interim recommendations developed by NVAC on priority groups for prophylaxis and treatment (see Part 1, Appendix D)
- Existing plans for emergency distribution of medical supplies (e.g., bioterrorism plans or SARS plans)

State-based planning for antiviral use should include obtaining antiviral drugs from national, state, and local stockpiles, and their distribution to priority groups by healthcare providers; data collection on drug use, drug-related adverse events, and drug resistance; coordination with bordering jurisdictions; legal preparedness; training; and dissemination of public health information.

These planning efforts require coordination and collaboration with healthcare providers who will administer antivirals during a pandemic. Examples of collaborative planning activities include:

- Convening local or state-wide pandemic influenza strategy meetings on the use of antivirals to facilitate local planning and define public- and private-sector roles (e.g., related to rapid administration to priority groups and medical surge capacity)
- Involving the local medical community (critical care, infectious disease, emergency medicine, and other specialties) in refining national guidelines for treatment and prophylaxis and providing information to the media and local populations on the appropriate use of antivirals
- Identifying contacts in tribal authorities and bordering states for coordinating distribution of antivirals (see below)

a) Procurement

Examples of planning steps for state-level procurement of antivirals include:

- Estimating the quantities of antiviral drugs that will be needed for treatment and prophylaxis of priority groups (see below)
- Identifying sources of antiviral drugs (e.g., state stockpiles, private sector, and federal supplies from the SNS). Drug procurement strategies might include:
  - Creating state or local stockpiles
  - Encouraging healthcare facilities to create institutional stockpiles
  - Making arrangements with local private-sector distributors for emergency purchase of antiviral drugs, if available

The establishment of state, local, or institutional stockpiles should take into account the expiration dates of the purchased material. All drugs are marked with an expiration date, based on review of stability data, at the time of manufacture. However, when purchased, the drugs might have been stored for some time in warehouses so that the time to expiration might be shorter than the time from initial manufacture to expiration date. Moreover, one shipment might consist of several batches with different expiration dates. Antivirals maintained in the national stockpile may be tested for potency and dating extended under the FDA shelf life extension program. Currently, state stockpiles are not included in this program.

b) Establishing priority groups

Based on interim recommendations on priority groups for antiviral treatment and prophylaxis (see Part 1, Appendix D), state and local health authorities should determine how certain priority groups (e.g., public safety workers, essential service providers, key decision makers) will be defined in their jurisdictions.

The Department of Defense (DoD) has purchased a supply of antivirals for use during a pandemic. Should the pandemic occur before the stockpile is received, DoD may require a portion of the national stockpile to treat or protect personnel in order to continue current combat operations and to preserve critical components of the military medical system. Should the military stockpile be exhausted and additional antiviral medication required to ensure national defense or continued support to civil authorities, use of antiviral drugs from the national stockpile may also be required.

c) Distributing and dispensing antivirals to priority groups

Planning steps for distribution of antivirals to priority groups might include:

- Estimating the size and needs of priority groups in local jurisdictions, using interim recommendations
- Assessing antiviral stocks available at the state, local, and hospital levels
- Establishing a mechanism to request antivirals from the federal stockpile, if needed (see below)
- Activating pre-existing plans for the transport, receipt, storage, security, tracking, and delivery of:
  - Antiviral stocks for use in treatment to hospitals, clinics, nursing homes, alternative care facilities, and other healthcare institutions. Prompt dispensing to point-of-care locations is crucial, because clinical efficacy for these agents has been demonstrated when treatment begins within 48 hours of the onset of symptoms.
  - Antiviral stocks for use in post-exposure prophylaxis (e.g., for direct contacts of infected patients)
  - Antiviral stocks for use in prophylaxis (e.g., if recommended for healthcare workers, public safety workers, and essential service providers)
- Considering the use of standing orders for treatment of certain priority groups, such as hospitalized patients and healthcare workers
- Developing a communication plan to explain the rationale for establishing these target groups (see also **Supplement 10**)

The decision to deploy federal assets from the SNS during an influenza pandemic will be made by HHS officials, as it would be during any public health emergency. Each state and federal agency with direct patient care responsibilities should designate a representative (e.g., the state epidemiologist or public health director) to make emergency requests for federal assets in the SNS.

Federal supplies of antivirals will be delivered to a site designated by state planners in each state or large city (e.g., state health department; existing SNS receipt, storage, staging site). State SNS coordinators should provide logistical guidance on the receipt and distribution of federal assets to priority groups.

d) Monitoring and data collection

To ensure optimal use of antiviral drugs during an influenza pandemic, state and local health departments and healthcare partners should work with federal officials and collect data on:

- Distribution of state or federal supplies of antiviral drugs
- Occurrence of adverse events following administration of antiviral drugs

State and local departments could also participate in federal efforts to collect data on:

- Effectiveness of treatment and prophylaxis
- Development of drug resistance

(1) Distribution. Allocation and distribution of antiviral drugs from state and local health departments to drug delivery or dispensing sites will be established based on state and local pandemic plans. Health departments should develop strategies to monitor drug distribution and use, assessing whether drugs are being effectively targeted to priority groups and whether distribution is equitable within those groups (e.g., among racial and ethnic minorities and persons of different socioeconomic levels).

(2) Antiviral effectiveness. Studies to evaluate the effectiveness of antiviral drug use during a pandemic will be conducted by federal agencies in collaboration with state and local health departments and other healthcare and academic partners. The effectiveness of antiviral therapy and prophylaxis will be assessed by comparing rates of severe influenza-related illness and death among treated and untreated persons and among persons who did and did not receive prophylaxis. Analyses of antiviral drug effectiveness should take into account characteristics that will vary among individuals and those that may vary over time, such as diagnostic practices, length of time to initiate therapy, and changes in the pandemic virus.

(3) Adverse events. Serious adverse events associated with the use of antiviral drugs for prophylaxis and treatment of influenza should be reported to FDA, using the MedWatch monitoring program. During an influenza pandemic, state and local health departments can assist in this effort by providing protocols and information to healthcare providers and encouraging hospitals to download MedWatch forms (available at http://www.fda.gov/medwatch/) for distribution to patients. Adverse events reported to MedWatch are collated and analyzed by FDA's Adverse Events Reporting System (AERS).

Use of antivirals will be much greater during a pandemic than during a regular influenza season.. To help improve the detection of serious adverse effects (especially rare effects or effects in vulnerable populations), additional efforts to encourage recognition and reporting of adverse events will be needed. These efforts might include:

- Active monitoring for adverse events observed at emergency rooms, through the National Electronic Injury Surveillance System Cooperative Adverse Drug Event project (NEISS-CADE)
- Local campaigns to educate healthcare workers about the recognition and reporting of adverse events
- Distribution of MedWatch forms and descriptions of known adverse events to each end-user who receives antiviral drugs

In addition, CDC, FDA, and AHRQ will explore the use of existing drug-monitoring systems that have access to individual health utilization records that may allow active, population-based surveillance for adverse events following the use of antivirals for treatment or prophylaxis.

(4) Antiviral drug resistance. CDC will work with state and local partners to monitor the development of resistance to antivirals. Because resistance to M2 inhibitors may involve a single base pair change, resistance may develop rapidly if these drugs are used widely. Information about resistance to M2 inhibitors and neuraminidase inhibitors can be found in the July 2005 recommendations of the ACIP http://www.cdc.gov/mmwr/PDF/rr/rr5408.pdf .

Global surveillance for neuraminidase resistance during a pandemic will also be conducted by the Neuraminidase Inhibitor Susceptibility Network (NISN). The global NISN was established in 1999 to address public health and regulatory concerns regarding the potential emergence and consequences of drug resistance in influenza viruses following the introduction of the influenza neuraminidase inhibitor (NI) class of antiviral agents. The Network includes representatives of each of the four WHO global influenza reference laboratories and scientists from regions of the world where increasing use of these drugs is anticipated.

CDC will test the drug susceptibilities of viruses isolated from different age groups and geographic groups over the course of the pandemic (see Antiviral Effectiveness above). State and local health departments should encourage clinicians to obtain specimens from patients who develop severe disease while receiving treatment or prophylaxis. State health departments should provide these specimens on a periodic basis, preferably after testing them by RT-PCR, viral culture, or rapid diagnostic testing to confirm the presence of strains of influenza A (see **Supplement 2**).

Surveillance for antiviral resistance may be particularly important during the later stages of the pandemic, especially if M2 agents have been widely used. Under these circumstances, the detection of widespread M2 inhibitor resistance might require a re-evaluation of priorities for prophylaxis and treatment.

e) Coordination with bordering jurisdictions

State and local health departments should review and coordinate antiviral drug distribution plans with health authorities in bordering jurisdictions, including:

- Counties
- States
- Tribal governments and other unique populations

During an influenza pandemic, states should share details regarding their distribution of antivirals with bordering jurisdictions to optimize targeting of antiviral use and clarify, in advance, any apparent inconsistencies in proposed policies.

f) Legal preparedness

State and local health departments should ensure that appropriate legal authorities are in place to facilitate implementation of plans for distributing antivirals. For example, if a state plan includes a provision for the state health commissioner to issue a blanket prescription for dispensing of antivirals, then the state health officer will need the authority and the plan will need to be consistent with state prescription laws. In addition, legal issues may include reviewing worker's compensation laws to determine how they apply to healthcare workers and other essential workers who take antivirals for prophylaxis.

g) Training

State and local health departments should enhance training and education efforts related to use of antiviral drugs during a pandemic. Exercises that involve healthcare providers who will administer antivirals to individual patients are essential to ensure that distribution systems are in place and that roles and responsibilities are well understood. It may be useful, for example, to provide healthcare providers with educational materials and to practice emergency distribution of antiviral drugs to target groups.

h) Public health information

State and local health departments should develop and implement plans to educate the public, the medical community, and other stakeholders about:

- Role of antivirals in responding to pandemic influenza
- Need to prioritize use of limited antiviral supplies for treatment and prophylaxis
- Rationale for the priority groups identified in the interim recommendations
- Importance of appropriate use (i.e., using the drugs as prescribed and for the full number of days recommended) to minimize the development of drug resistance

i) Contingency planning for Investigational New Drug (IND) use

State and local health departments should be prepared to distribute unlicensed antiviral drugs (if needed) under FDA's Investigational New Drug (IND) provisions. IND provisions require strict inventory control and recordkeeping, completion of a signed consent form from each person who receives the medication, and mandatory reporting of specified types of adverse events. IND provisions also require approval of the protocol and consent form by an Institutional Review Board (IRB). The FDA regulations permit the use of a national or "central" IRB. A treatment IND is one IND mechanism that FDA has available for use and is especially suited for large scale use of investigational products. http://www.access.gpo.gov/nara/cfr/waisidx_99/21cfr_99.html

As an alternative to IND use of an unapproved antiviral drug, HHS may utilize the drug product under Emergency Use Authorization procedures as described in the FDA draft Guidance "Emergency Use Authorization of Medical Products" http://www.fda.gov/cber/gdlns/emeruse.pdf

S7-IV. Recommendations for the Pandemic Period

Interim recommendations for use of antivirals may be updated throughout the course of an influenza pandemic to reflect current epidemiologic and laboratory data. Interim recommendations may also be updated as an effective influenza vaccine becomes available.

A. When pandemic influenza is reported abroad, or sporadic pandemic influenza cases are reported in the United States, without evidence of spread

If an influenza pandemic has begun in other countries, state and local health departments should:

- Use antiviral drugs in the management of persons infected with novel strains of influenza and their contacts, as described in S7-III.A or its updates.
- Work with healthcare partners to consider providing antiviral prophylaxis to persons at highest risk for pandemic influenza. Examples of such persons include:
  - Public health workers who investigate suspected cases of pandemic influenza
- Meet with local partners and stakeholders to review the state-based antiviral drug distribution plan (see S7-III.B). As part of this effort, state and local partners could:
  - Modify the distribution plan to take into account possible updated recommendations on target groups and updated information on projected supplies of antiviral drugs.
  - Notify the medical community about the status of the plan and the availability of antiviral drugs.
  - Disseminate public health guidelines that encourage drug-use practices that help minimize the development of drug resistance.
  - Provide the public with information on interim recommendations and their rationale for the use of antiviral drugs during an influenza pandemic.
- Work with federal partners to monitor the safety and effectiveness of drugs and ensure that available antivirals are used in accordance with federal and local recommendations.

B. When there is limited transmission of pandemic influenza in the United States

When there is limited transmission of pandemic influenza in the United States, state and local health departments should:

- Activate state-based plans for targeting antiviral drugs to priority groups for prophylaxis and treatment (see S7-III.B).

- Request antiviral drugs, as needed, from previously identified sources (see S7-III.B), including the SNS.
- Continue to work with healthcare partners to ensure appropriate use of antivirals in the medical management of early cases and contacts (see S7-IV.A).
- Assist hospitals in implementing procedures for early detection and treatment of influenza in healthcare workers (see **Supplement 3**).
- Work with federal partners to begin monitoring the safety and effectiveness of drugs and ensure that available antivirals are used in accordance with federal and local recommendations.

C. When there is widespread transmission of pandemic influenza in the United States

When transmission of pandemic influenza has become widespread, the paramount goals of antiviral use will be to treat those at highest risk of severe illness and death and to preserve the delivery of healthcare and other essential critical services through early treatment and limited prophylaxis.

After a vaccine becomes available, antiviral drugs may be used to protect persons who have an inadequate vaccine response (e.g., the elderly and those with underlying immunosuppressive disease) as well as persons with contraindications to vaccination, such as anaphylactic hypersensitivity to eggs or other vaccine components.

Until the pandemic has waned, state and local health departments should continue to work with healthcare and federal partners to monitor the safety and effectiveness of antivirals and to encourage appropriate drug use practices that help minimize the development of drug resistance.

BOX 1. STRATEGIES FOR ANTIVIRAL USE IN PANDEMIC INFLUENZA TREATMENT AND PROPHYLAXIS

The goals of vaccine and antiviral use during an influenza pandemic are to limit mortality and morbidity, minimize social disruption, and reduce economic impact. Because a pandemic vaccine is unlikely to be available during the first 4 to 6 months of the pandemic, appropriate use of antivirals may play an important role in achieving these goals.

A. Treatment

1. Planning considerations

- The effectiveness of antivirals against a new pandemic influenza virus cannot be predicted.
- Pooled analyses of clinical trials of neuraminidase inhibitors administered to outpatients with seasonal influenza suggest that early treatment may reduce the risk of hospitalization by ~50%. There are no data on the effectiveness of neuraminidase inhibitors in preventing either serious morbidity (e.g., requirement for intensive care) or mortality (see July 2005 recommendations of the AHIC (http://www.cdc.gov/mmwr/PDF/rr/rr5408.pdf).
- Antiviral agents used against seasonal influenza have demonstrated efficacy in clinical trials when treatment is initiated within 48 hours of the onset of symptoms. Assuming that they have a similar level of effectiveness against pandemic influenza, rapid diagnosis, distribution and administration of antivirals during a pandemic will be essential.
- Early treatment is a more efficient use of antivirals than widespread prophylaxis. Because prophylaxis for approximately 6 weeks would require at least four times the number of doses as a 5-day treatment course per individual, huge antiviral stockpiles would be required to permit prophylaxis of more than a small proportion of the U.S. population.
- Most influenza A(H5N1) viruses currently in circulation in southeast Asia are resistant to the M2 ion channel inhibitors (amantadine and rimantadine), and strains that may evolve from these viruses may become resistant to this class of antivirals.

The emergence of drug resistant strains is less likely during treatment with neuraminidase inhibitors (oseltamivir and zanamivir) than with M2 inhibitors (amantadine and rimantadine). Neuraminidase inhibitors may also have a lower incidence of severe side effects (see July 2005 recommendations of the AHIC (http://www.cdc.gov/mmwr/PDF/rr/rr5408.pdf). Oseltamivir and zanamivir should therefore be reserved for treatment whenever possible. Because supplies of oseltamivir and zanamivir are currently depleted, early depletion of oseltamivir and widespread use of M2 inhibitors could lead to increased rates of side effects and drug resistance.

2. Strategies for treatment

Treatment strategies for optimizing the use of limited stocks of antiviral drugs will vary depending on the phase of the pandemic. The following interim guidance will be updated as more information becomes available. Strategies for consideration include:

At all stages of a pandemic:

- Targeting therapy to influenza patients admitted to a hospital who present within 48 hours of symptom onset.
- Implementing mechanisms to detect the emergence of drug-resistant variants of a pandemic influenza strain (e.g., obtaining specimens from persons who develop influenza while on prophylaxis or who progress to severe disease despite treatment).

BOX 1. STRATEGIES FOR ANTIVIRAL USE IN PANDEMIC INFLUENZA TREATMENT AND PROPHYLAXIS (CONT.)

During the earliest stages of a pandemic in the United States:

- Basing treatment decisions on laboratory-confirmed subtype identification of the pandemic strain by viral isolation, RT-PCR, or other means recommended by CDC. A positive rapid antigen test for influenza A would be sufficient grounds for initiating treatment, with a confirmatory, definitive laboratory test required for continuation of treatment.
- Interpreting negative results of influenza testing as permitting termination of treatment, given the overall low rate of infection in a particular community.
- Considering targeted use of antivirals to contain small, well-defined disease clusters, to possibly delay or reduce spread to other communities (see also Part C [below] and Supplement 8).

When there is increasing disease activity in the United States:

- Basing treatment decisions on:
  - Laboratory-confirmed identification of the pandemic subtype by viral isolation and subtyping, RT-PCR, or other means recommended by CDC, *or*
  - Detection of influenza A by rapid antigen test, *or*
  - Epidemiologic and clinical characteristics.
- Permitting initiation of antiviral treatment before results from viral isolation, IFA, RT-PCR assays, or rapid antigen tests become available, since early treatment is more likely to be effective.

Once infection becomes more common, negative rapid antigen test results are more likely to represent false negatives; therefore, treatment should continue while awaiting results from confirmatory testing.

When the pandemic is widespread in the United States:

- Basing treatment decisions on clinical features and epidemiologic risk factors, taking into account updated knowledge of the epidemiology of the pandemic virus.

As the pandemic progresses, strategies for antiviral treatment may be revised as new information is obtained about the pandemic strain.

B. Prophylaxis

1. Planning considerations for prophylaxis

- Primary constraints on the use of antivirals for prophylaxis will be:
  - Limited supplies
  - Increasing risk of side effects with prolonged use
  - Potential emergence of drug-resistant variants of the pandemic strain, particularly with long-term use of M2 inhibitors
- The need for antiviral prophylaxis may decrease once an effective pandemic influenza vaccine becomes available for use among healthcare workers and other groups receiving prophylactic antivirals.

BOX 1. STRATEGIES FOR ANTIVIRAL USE IN PANDEMIC INFLUENZA TREATMENT AND PROPHYLAXIS (CONT.)

- Post-exposure prophylaxis might be useful in attempts to control small, well-defined disease clusters (e.g., outbreaks in long-term care facilities [see section C below]). A study of post-exposure prophylaxis using amantadine—conducted during the 1968 pandemic—demonstrated little effectiveness, possibly due to rapid development of resistance (see July 2005 recommendations of the AHIC (http://www.cdc.gov/mmwr/PDF/rr/rr5408.pdf).
- Oseltamivir has demonstrated >70% efficacy as prophylaxis against laboratory-confirmed febrile influenza illness during interpandemic periods in unimmunized adults (see July 2005 recommendations of the AHIC (http://www.cdc.gov/mmwr/PDF/rr/rr5408.pdf).
- Prophylaxis with amantadine or rimandatine decreased the risk of influenza illness during the 1968 pandemic and the 1977 reappearance of H1N1 viruses (see July 2005 recommendations of the AHIC (http://www.cdc.gov/mmwr/PDF/rr/rr5408.pdf).
- The number of persons who receive prophylaxis with oseltamivir should be minimized, primarily to extend supplies available to treat persons at highest risk of serious morbidity and mortality. If sufficient antiviral supplies are available, prophylaxis should be used only during peak periods of viral circulation to protect small groups of front-line healthcare workers and other providers of essential community services prior to availability of vaccine.
- If a pandemic virus is susceptible to M2 ion channel inhibitors, amantadine and rimantadine should be reserved for prophylaxis, although drug resistance may emerge quickly.
- Rimantadine is preferred over amantadine, because it is associated with a lower incidence of serious side effects (see July 2005 recommendations of the AHIC (http://www.cdc.gov/mmwr/PDF/rr/rr5408.pdf). Strains that are resistant to one M2-class antiviral are likely resistant to the other.

2. Strategies for prophylaxis

Strategies for effective use of antiviral prophylaxis during a pandemic include:

- Targeting prophylaxis to priority groups (see Part 1, Appendix D for interim recommendations) throughout the first wave of the pandemic. Data from 20th century influenza pandemics suggest that the first wave of these pandemics lasted approximately 4 to 8 weeks in a community.
- Using post-exposure prophylaxis (generally for 10 days) to:
  - Control small, well-defined disease clusters, such as outbreaks in nursing homes or other institutions, to delay or reduce transmission to other communities (see part C above).
  - Protect individuals with a known recent exposure to a pandemic virus (e.g., household contacts of pandemic influenza patients).

When a vaccine becomes available, post-exposure prophylaxis may also be used to protect key personnel during the period between vaccination and the development of immunity.

Strategies for antiviral prophylaxis may be revised as the pandemic progresses, depending on supplies, on what is learned about the pandemic strain and on when a vaccine becomes available.

BOX 1. STRATEGIES FOR ANTIVIRAL USE IN PANDEMIC INFLUENZA TREATMENT AND PROPHYLAXIS (CONT.)

C. Strategies for Combined Treatment and Prophylaxis

During the Pandemic Alert Period, combined antiviral treatment for ill persons and targeted post-exposure prophylaxis of contacts might be considered in attempts to contain small disease clusters (e.g., institutional outbreaks or household introductions). The potential use of targeted prophylaxis to contain disease clusters is considered in **Supplement 8**.

The administration of oseltamivir does not interfere with the development of antibodies to influenza viruses after administration of trivalent inactivated influenza vaccine. Therefore, persons receiving prophylaxis can continue to receive oseltamivir during the period between vaccination and the development of immunity. Whether oseltamivir can interfere with the immune response elicited by a live-attenuated pandemic vaccine is unknown.

D. Pediatric Use

None of the available influenza antivirals are currently FDA approved for use among children aged <1 year. In particular, the safety and efficacy of oseltamivir have not been studied in children aged <1 year for either treatment or prophylaxis of influenza (see oseltamivir package insert). The decision by an individual physician to treat children aged <1 year in an emergency setting on an off-label basis with an antiviral must be made on a case-by-case basis with full consideration of the potential risks and benefits. Additional human data on the safety of these agents in the treatment of influenza in young children are needed.

Oseltamivir is available as an oral suspension for use in children. This formulation of oseltamivir may not be available in sufficient supply during a pandemic to treat all pediatric patients. If physicians consider opening 75 mg oseltamivir capsules and using the contents in an attempt to deliver a partial, pediatric dose to children, it must be recognized that there are insufficient data on palatability, stability, and dosing consistency to predict the safety or effectiveness of such unapproved use. Additional study of these issues is needed.

BOX 2. FEDERAL SUPPLIES OF ANTIVIRAL DRUGS IN THE STRATEGIC NATIONAL STOCKPILE

During an influenza pandemic, a decision to deploy federal assets from the Strategic National Stockpile (SNS) will be made by HHS. As of October 2005, the SNS (http://www.bt.cdc.gov/stockpile/) contained 2.26 million treatment regimens of oseltamivir (capsules and suspension), 5 million treatment regimens of rimantadine (tablets and syrup), and 84,000 treatment regimens of zanamivir. Two million additional oseltamivir courses will be delivered to the SNS by November 2005 and additional purchases of antivirals are pending.

The details of the HHS approach for allocation and distribution of SNS assets during an influenza pandemic are currently under consideration. State and local health departments and federal agencies with direct patient care responsibilities should begin to:

- Develop plans to allot antivirals to healthcare facilities, assuming that distribution of limited supplies of antivirals will initially be targeted to patients hospitalized with pandemic influenza and for treatment or prophylaxis of essential healthcare workers.
- Consider the use of standing orders for the prescription of antivirals, particularly for use in healthcare workers.
- Consider the use of occupational health clinics in hospitals and other healthcare organizations for delivery of antivirals to healthcare workers.

It is not recommended that individuals, fearing a pandemic, stockpile oseltamivir in homes or that healthcare providers prescribe oseltamivir to individuals for prophylaxis against pandemic influenza. At the present time, quantities are insufficient to address all of the interim pre-determined groups, and thus stockpiling oseltamivir will take away limited resources from those with highest priority.

TABLE 1. CHARACTERISTICS OF ANTI-INFLUENZA ANTIVIRAL DRUGS

	Inhibits	Acts on	Administration	Common Side Effects
Amantadine	M2 ion channel	Influenza A	Oral	CNS, GI
Rimantadine	M2 ion channel	Influenza A	Oral	CNS, GI (less often than amantadine)
Oseltamivir	Neuraminidase	Influenza A and B	Oral	GI
Zanamivir	Neuraminidase	Influenza A and B	Inhaler	Bronchospasm

These agents differ in mechanisms of action, pharmokinetics, FDA-approved indications, dosages, cost, and potential for emergence of drug resistance (see July 2005 recommendations of the AHIC (http://www.cdc.gov/mmwr/PDF/rr/rr5408.pdf).

The neuraminidase inhibitors and rimantadine are superior to amantadine with regard to the frequency of serious side effects.

The use of M2 inhibitors, particularly for treatment, is likely to lead to the emergence and spread of drug-resistant influenza viruses.

TABLE 2. RECOMMENDED DAILY DOSAGE OF ANTIVIRALS FOR TREATMENT AND PROPHYLAXIS

(From *Prevention and Control of Influenza Recommendations of the Advisory Committee on Immunization Practices [ACIP], July 2005*)

Antiviral Agent	Age Groups (years) 1–6	7–9	10–12	13–64	≥65
Amantadine[a]					
Treatment, influenza A	5mg/kg body weight/day up to 150 mg in two divided doses[b]	5mg/kg body weight /day up to 150 mg in two divided doses[b]	100 mg twice daily[c]	100 mg twice daily[c]	≤100 mg/day
Prophylaxis, influenza A	5mg/kg body weight /day up to 150 mg in two divided doses[b]	5mg/kg body weight /day up to 150 mg in two divided doses[b]	100 mg twice daily[c]	100 mg twice daily[c]	≤100 mg/day
Rimantadine[d]					
Treatment,[e] influenza A	NA[f]	NA	NA	100 mg twice daily[c,g]	100 mg/day
Prophylaxis, influenza A	5m/kg body weight /day up to 150 mg in two divided doses[b]	5mg/kg body weight /day up to 150 mg in two divided doses[b]	100 mg twice daily[c]	100 mg twice daily[c]	100 mg/day[h]
Zanamivir[i,j]					
Treatment, influenza A and B	NA	10 mg twice daily	10 mg twice daily	10 mg twice daily	10 mg twice daily
Oseltamivir					
Treatment,[k] influenza A and B	dose varies by child's weight[l]	dose varies by child's weight[l]	dose varies by child's weight[l]	75 mg twice daily	75 mg twice daily
Prophylaxis, influenza A and B	NA	NA	NA	75 mg/day	75 mg/day

NOTE: Amantadine manufacturers include Endo Pharmaceuticals (Symmetrel (R)–tablet and syrup) and Geneva Pharms Tech (Amantadine HCL–capsule); USL Pharma (Amantadine HCL–capsule and tablet); and Alpharma, Carolina Medical, Copley Pharmaceutical, HiTech Pharma, Mikart, Morton Grove, and Pharmaceutical Associates (Amantadine HCL–syrup), and Sandoz. Rimantadine is manufactured by Forest Laboratories (Flumadine (R)–tablet and syrup); Corepharma , Impax Labs (Rimantadine HCL–tablet), and Amide Pharmaceuticals (Rimantadine HCL–tablet). Zanamivir is manufactured by GlaxoSmithKline (Relenza (R)–inhaled powder). Oseltamivir is manufactured by Roche Pharmaceuticals (Tamiflu (R)–tablet). Information based on data published by the U.S. Food and Drug Administration at www.fda.gov, accessed 3/30/2005.

[a] The drug package insert should be consulted for dosage recommendations for administering amantadine to persons with creatinine clearance ≤50 ml/min/1.73m2 .

[b] 5 mg/kg body weight of amantadine or rimantadine syrup = 1 tsp/2.2 lbs.

[c] Children aged ≥10 years who weigh <40 kg should be administered amantadine or rimantadine at a dosage of 5 mg/kg body weight /day.

[d] A reduction in dosage to 100 mg/day of rimantadine is recommended for persons who have severe hepatic dysfunction or those with creatinine clearance ≤10 mL/min. Other persons with less severe hepatic or renal dysfunction taking 100 mg/day of rimantadine should be observed closely, and the dosage should be reduced or the drug discontinued, if necessary.

[e] Approved by FDA only for treatment among adults.

[f] Not applicable.

[g] Rimantadine is approved by FDA for treatment among adults. However, certain experts in the management of influenza consider it appropriate for treatment among children. (See American Academy of Pediatrics, 2003 Red Book.)

[h] Older nursing-home residents should be administered only 100 mg/day of rimantadine. A reduction in dosage to 100 mg/day should be considered for all persons aged ≥65 years if they experience possible side effects when taking 200 mg/day.

[i] Zanamivir administered via inhalation using a plastic device included in the medication package. Patients will benefit from instruction and demonstration of the correct use of the device.

[j] Zanamivir is not approved for prophylaxis.

[k] A reduction in the dose of oseltamivir is recommended for persons with creatinine clearance <30 ml/min.

[l] The dose recommendation for children who weigh ≤15 kg is 30 mg twice a day. For children who weigh >15 to 23 kg, the dose is 45 mg twice a day. For children who weigh >23 to 40 kg, the dose is 60 mg twice a day. And for children who weigh >40 kg, the dose is 75 mg twice a day.

supplement 8
community disease control and prevention

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S8-I. RATIONALE

The initial response to the emergence of a novel influenza subtype that spreads between people should focus on containing the virus at its source, if feasible, and preventing a pandemic. Once spread beyond the initial focus occurs and with introduction of the virus into the United States, the foci of containment activities will be public health and individual measures that attempt to slow and limit viral transmission. For the purposes of this document, containment measures refer to measures that attempt to fully limit transmission as well as those that attempt to slow transmission. Containment strategies aimed at controlling and slowing the spread of the virus might include measures that affect individuals (e.g., isolation of patients and monitoring their contacts) as well as measures that affect groups or entire communities (e.g., cancellation of public gatherings; implementation of community-wide snow days). Guided by epidemiologic data, state and local authorities will implement the most appropriate of these measures in efforts to maximize impact on disease transmission and minimize impact on individual freedom of movement. HHS will provide assistance to states and localities as requested, including sharing experience of others and providing advice on decision-making as the situation evolves. Although states and localities have primary responsibility for public health matters within their borders, including isolation and quarantine, under the authority of Section 361 of the Public Health Service Act (42 USC 264), the HHS Secretary may make and enforce regulations necessary to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the United States or from one state or possession into another.

Containment measures applied to individuals (e.g., isolation and quarantine) may have limited impact in preventing the transmission of pandemic influenza, due to the short incubation period of the illness, the ability of persons with asymptomatic infection to transmit virus, and the possibility that early symptoms among persons infected with a novel influenza strain may be non-specific, delaying recognition and implementation of containment. Nevertheless, during the Pandemic Alert Period with a less efficiently transmitted virus, these measures may have great effectiveness, slowing disease spread and allowing time for targeted use of medical interventions. In addition, implementing these measures early in a pandemic when disease is first introduced into the U.S. and when the scope of the outbreak is focal and limited may slow geographical spread and increase time for vaccine production and implementation of other pandemic response activities. Later, when disease transmission is occurring in communities around the U.S., individual quarantine is much less likely to have an impact and likely would not be feasible to implement. Thus, community-based containment measures (e.g., closing schools or restricting public gatherings) and emphasizing what individuals can do to reduce their risk of infection (e.g., hand hygiene and cough etiquette) may be more effective disease control tools.

Although there are few data from past pandemics to guide containment efforts, the potential effectiveness of strictly implemented movement restrictions is supported by historical accounts that describe the use of such measures in American Samoa and in some Alaskan villages during the pandemic of 1918-1919. American Samoa banned inbound and outbound travel and mail service and (unlike Western Samoa) remained influenza-free. In Alaska, quarantine and isolation measures apparently delayed introduction of pandemic influenza into the Alaskan interior for several months, and some isolated villages were completely spared. Today, much more extensive international and domestic travel and the interdependence between communities make it unlikely that strict restrictions could be effectively imposed and that, except in unique settings, communities could prevent outbreaks from occurring. Preliminary mathematical modeling results suggest that travel restrictions would need to be about 99% effective to delay introduction into a country by one to two months. Based on these results, the goals of containment activities during a pandemic should be to slow the spread of disease early after introduction into the U.S. and to limit the number of persons who become infected in community outbreaks throughout the pandemic.

S8-II. OVERVIEW

Supplement 8 provides recommendations to state and local partners on the use of disease containment strategies to prevent or decrease transmission at different phases of an influenza Pandemic Alert Period and Pandemic Period. Recommendations for the Interpandemic and Pandemic Alert Periods focus on preparedness planning for implementation of containment measures. They also outline actions that may be taken during the earliest stage of a pandemic when the first potential cases or disease clusters are detected. In this setting, individual-level containment measures (e.g., patient isolation and identification, monitoring, quarantine of contacts) may be useful in slowing the spread of pandemic influenza and may be used without causing undue strain on limited public heath and other healthcare resources.

Recommendations for the Pandemic Period focus on measures that may be beneficial and practical when there is a large number of cases and extensive viral transmission. In such a setting, individual-level measures may no longer be effective or feasible (e.g., if most contacts cannot be traced in time to prevent further exposures; if staffing constraints make contact tracing impractical). In this setting, state and local health departments might consider measures that decrease social contact within groups or whole communities (e.g., self-shielding, cancellation of public events, snow days, quarantine of groups of exposed persons, widespread community quarantine). Effective use of community containment measures during a pandemic will require periodic assessment of the properties of the pandemic virus and the distribution and clinical presentation of the cases. Guidance on containment recommendations will be updated, as needed.

S8-III. RECOMMENDATIONS FOR THE INTERPANDEMIC AND PANDEMIC ALERT PERIODS

A. Community preparedness for implementation of pandemic influenza containment measures

Both individual and community-based containment measures raise legal, logistic, and social challenges that should be addressed during the Interpandemic Period. This section provides information on planning for disease control and containment, legal preparedness, planning for potential use of influenza hotlines (preparing for influenza clinics is discussed in **Supplement 3**), and the role of communications in preparing the public to accept the possible need for restrictive measures to reduce the spread of pandemic influenza. Appendix 2 provides additional guidance on these topics, as well as on preparedness activities related to management of cases and contacts, non-hospital-based isolation of cases, and implementation of community containment measures. Information on hospital preparedness for patient isolation is provided in **Supplement 3.**

1. Planning for disease control and containment

Experience during the 2003 SARS outbreak (Appendix 3) suggests that local officials will face logistic, economic, ethical, legal, social, and psychological challenges in implementing disease control and containment measures during a Pandemic Alert and Pandemic Period. Although individual quarantine as a control measure is likely only to be used during the Pandemic Alert and very early during the Pandemic Period—for example, among communities where initial cases are introduced into the U.S.—all state and local health departments and tribal authorities should anticipate and prepare for the challenges of effectively implementing this measure by working with community partners to review the steps involved in establishing and maintaining quarantine facilities and procedures.

Key activities include (see Appendix 2):

- Identifying and engaging traditional partners (e.g., public heath and healthcare workers) and non-traditional community partners (e.g., transportation workers) and inviting them to participate in preparedness planning and in pandemic influenza containment exercises and drills
- Identifying potential isolation and quarantine facilities

- Establishing procedures for medical evaluation and isolation of quarantined persons who exhibit signs of influenza-like illness (ILI)
- Developing tools and mechanisms to prevent stigmatization and provide mental health services to persons in isolation or quarantine, as well as to family members of affected persons and other community members
- Establishing procedures for delivering medical care, food, and services to persons in isolation or quarantine. These efforts should take into account the special needs of children and persons with disabilities.
- Developing protocols for monitoring and enforcing quarantine measures
- Ensuring legal authorities and procedures exist for various levels of movement restrictions
- Establishing procedures for issues related to employment compensation and job security

2. Legal preparedness

States, localities, and tribes have primary responsibility for public health matters within their borders, including isolation and quarantine. Current quarantine laws, regulations, and enforcement procedures vary widely from state to state. Many of these laws date to the 19th century. In response to a request from CDC, the Center for Law and the Public's Health at Georgetown and Johns Hopkins universities has developed a draft Model State Emergency Health Powers Act (www.publichealthlaw.net/MSEHPA/MSEHPA2.pdf) to assist state and local health agencies in reviewing emergency public health powers to ensure they are adequate to respond to modern disease and bioterrorism concerns.

Under the authority of Section 361 of the Public Health Service Act (42 USC 264), the HHS Secretary may make and enforce regulations necessary to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the United States or from one state or possession into another. Under authority delegated by the HHS Secretary, the CDC Director may isolate and quarantine persons who have been exposed to or are infected with certain specified communicable diseases and are arriving into the United States from a foreign country or traveling from one state or possession into another (42 CFR 71.32(a) & 42 CFR 70.6). The communicable diseases for which individuals may be subject to federal quarantine are specified in an Executive Order of the President, upon recommendation of the HHS Secretary in consultation with the Surgeon General. The most recent Executive Order is Executive Order 13295 of April 4, 2003, as amended by Executive Order 13375 of April 5, 2005. The April 5 amendment added influenza that is causing or has the potential to cause a pandemic to the list of federal quarantinable diseases (http://www.cdc.gov/ncidod/dq/index.htm). In addition, under section 311 of the PHS Act (42 USC 243), HHS may cooperate with and aid state and local authorities in the enforcement of their quarantine and other health regulations.

New International Health Regulations (IHR) were recently adopted by the World Health Assembly, which requires member states to report cases of human infection caused by a new subtype. When WHO has determined that a particular event constitutes a public health emergency, the IHR require WHO to make a"real-time" response to the emergency. Based on the details specific to the emergency, the Director General of WHO will recommend measures for implementation by the affected state as well as by other states. These time-limited recommendations are made available to states and, subsequently, made public. Depending on the evidence, recommended measures could be modified or ended.

3. Planning for influenza clinics and hotlines

An influenza pandemic is likely to put great stress on the healthcare delivery system, in particular emergency departments. To prevent overwhelming demand from compromising the function of emergency departments, healthcare providers, organizations, and public health authorities should consider optimal methods for delivering assessment and care to individuals with probable influenza. This may include designating certain offices or clinics or otherwise discrete areas for screening, triage, and care of individuals with influenza-like illness. While the large majority of outpatient care during a pandemic will be provided by patients' usual medical care practitioner, health authorities may decide to establish special facilities (*influenza clinics*) to provide rapid medical assessment of potentially infected persons, as part of efforts to control and contain small,

well defined disease clusters (see S8-III.C), or in geographical areas that are medically underserved. Ill persons will be encouraged to call special *influenza hotlines* that provide advice on whether to stay home or to seek medical care. Local public health systems supporting hotlines as triage and information systems must be aware of the healthcare resources available in the community. These "community triage" efforts may help prevent hospitals from being overwhelmed with patients who do not require hospital-level care. Moreover, community triage efforts may also reduce the number of uninfected persons who mingle with infected persons at clinics and hospitals. Preparedness planning for establishing influenza hotlines includes:

- Establishing telephone hotline numbers that people can call to report specific symptoms (e.g., fever) that will be specified by the state health department and CDC
- Identifying sites, staff members, and volunteers
- Developing protocols for hotline staff members that include training components and triage decision trees or algorithms
- Establishing communication systems with influenza clinics, if they are established

Organization of outpatient care in a community and potential establishment of influenza clinics is discussed in **Supplement 3**.

4. Public understanding of disease containment measures

Community preparedness for implementation of both individual and community control measures can be enhanced during the Interpandemic Period by improving public understanding of the dangers of pandemic influenza and the benefits of community-wide disease control practices, including social-distancing measures that can prevent illness and death (Appendix 4). Strategies for disease control will be facilitated by clear communication of the rationale for—and duration of—containment measures.

Local public health education campaigns that involve community partners can build public confidence in the ability to cope with an influenza pandemic. Partners may include schools, faith-based organizations, community-based organizations, and other "civil society" institutions that can help educate the public and provide support to families and persons who are incapacitated by illness.

Local public health campaigns should explain how individual action (e.g., strict compliance with respiratory hygiene, staying home when ill) and community efforts (e.g., implementation of snow days and self-shielding) can help reduce disease transmission. Education campaigns can describe the criteria, justification, role, methodology, and duration of quarantine and the social, medical, and psychological ways in which persons will be supported during the quarantine period. They can also explain that quarantine—which temporarily restricts personal movement—is a collective action implemented for the common good. In addition, they can allay public concerns about privacy issues related to the provision of medical information to healthcare workers and public health officials. These key messages should be translated and modified as required to address the cultural and linguistic needs of local neighborhoods.

Key messages prepared for use during the Interpandemic Period can be adapted for use during an actual pandemic (see Appendix 5 and **Supplement 10.**)

5. Enforcement and support of community containment measures

Experience from the 2003 SARS outbreak suggests that quarantine applied on a voluntary basis can be sufficient to reduce disease transmission (see Appendix 3). This idea is in accordance with data from modeling studies that suggest that quarantine and other community-based measures may be effective even if compliance is less than perfect.[1] Nevertheless, states, localities, and tribes should be prepared to enforce individual and community-based containment measures, if needed. The role of other Federal agencies in enforcing community containment measures will be detailed in the Federal Pandemic Influenza Plan.

[1] Meltzer MI, Damon I, LeDuc JW, Millar JD. Modeling potential responses to smallpox as a bioterrorist weapon. EIF.2001. Nov-Dec:7(6):959-69.

B. Management of patients infected with novel strains of influenza and their contacts

In this document, the term "novel strains of influenza" is used to refer to avian or animal influenza strains that can infect humans (like influenza A [H5N1]) and new or reemergent human viruses that cause cases or clusters of human disease. Guidance on the detection and identification of persons who might be infected with novel strains of influenza is provided in **Supplement 1**. Guidance on the clinical management of persons with novel influenza infection is provided in **Supplement 5**.

The choice of measures to contain the spread of novel strains of influenza during the Pandemic Alert Period will vary depending on the assessment of risk, as reflected in the three Pandemic Alert Phases described by WHO (Box 2).

1. Patient isolation

Infection control precautions and procedures for isolating influenza patients—at home or in a residence, community facility, or hospital—are described in Supplement 4. The patient will be admitted to a hospital if clinically indicated, if public health needs require it, or if isolation at home or in a community facility cannot be achieved safely and effectively. Information for evaluating the suitability of homes and facilities for patient isolation is provided in Appendix 6.

The state or local health department, in consultation with federal agencies, will advise the healthcare provider and healthcare facility on additional steps that may be taken, before and after laboratory test results become available, via the state public health laboratory or CDC.

2. Management of close contacts

In most situations—even at the earliest stages of a pandemic—it will not likely be possible to trace and quarantine close contacts of suspected or confirmed cases within 48 hours (the average incubation period for human influenza). However, in certain situations, especially during the later phases of the WHO Pandemic Alert Period (Box 2), efforts to identify exposed individuals or groups might be recommended. Examples might include:

- Suspected or confirmed cases of novel influenza. For example, a suspected or confirmed case of avian influenza A (H5N1) in persons who have traveled to an H5N1-affected country and have been exposed to sick poultry (either through handling or eating poultry products) or a laboratory-confirmed human case of H5N1 influenza
- Suspected or confirmed cases of avian influenza A (H5N1) or another novel strain of influenza in travelers on airplanes or cruise ships about to arrive in the United States (see **Supplement 9**)
- Suspected or confirmed cases of avian influenza of any type in persons with known exposure to sick poultry or birds in the United States
- Clusters of avian influenza A (H5N1) or another novel strain of influenza in small, well defined settings, such as a military base
- Cases of laboratory exposure to avian influenza A (H5N1) or influenza viruses with the potential to cause a pandemic (e.g., influenza A [H2N2])

Decisions on whether to trace a patient's contacts and how to manage them will be made on a case-by-case basis by local and/or state public health departments, in consultation with CDC, taking into consideration:

- Likelihood that the suspected case is due to a novel influenza strain (based on symptoms and travel history, if laboratory results are not yet available)
- Likelihood that the causative virus is transmitted from person-to-person with a moderate or high efficiency (as reflected in the designated Pandemic Alert phase)

- Feasibility of conducting contact-tracing given the short incubation period for influenza

A patient's close contacts may include family, friends, work colleagues, classmates, fellow passengers, and/or healthcare providers. Management of contacts might include passive or active monitoring without activity restrictions and/or quarantine at home or in a designated facility. In the Pandemic Alert Period, especially during Phase 3 or 4 when little or limited person-to-person transmission has been documented, quarantine of contacts should be implemented **only when there is a high probability that the ill patient is infected with a novel influenza strain that may be transmitted to others**.

Contacts who are quarantined should be monitored by a health department official (or designee) at least once a day—by phone or in person—to assess symptoms and address any needs. Frequent monitoring (e.g., twice a day) will facilitate early detection, reducing the interval between the onset of symptoms and the isolation of the sick person. Early signs of influenza include fever, respiratory symptoms, and chills, rigors, myalgia, headache, or diarrhea. Quarantine may be lifted as soon as the exposed contact has remained without signs or symptoms of disease for a complete incubation period for influenza disease. (Experience with seasonal influenza suggests the incubation period is 1-4 days, with an average length of 2 days. However, the clinical behavior of a novel influenza virus may be different and could potentially be as long as 10 days. Pandemic influenza preparedness activities should plan for containment measures that may last between 1-10 days. For the purposes of this document, 10 days is referred to as the incubation period; however, public health authorities should be prepared to adjust the time frame as more is known about the virus.) Additional information on monitoring and evaluating persons in quarantine is provided in Appendix 6.

3. Data collection

Public health officials or designees should collect information on cases and contacts, including:

- Number of contacts identified per case
- Information on each contact:
  - Relationship to the case-patient
  - Nature and time of exposure
  - Whether the contact was vaccinated or on antiviral prophylaxis
  - Underlying medical conditions
- Number of contacts (including any in quarantine) that become ill
- Number of days between onset of symptoms and reporting to health officials

  These data will guide decision-making on whether to implement more stringent containment measures.

C. Containment of small clusters of infection with novel strains of influenza

Community-based control measures that state and local health officials might use to contain small clusters of infection with novel strains of influenza (during the later Pandemic Alert phases or when cases are first introduced into the U.S.) include targeted chemoprophylaxis and early detection of new cases by use of influenza hotlines and clinics. These approaches may be implemented in small, well defined settings. They are not likely to be useful once a pandemic is underway.

1. Targeted chemoprophylaxis of disease clusters

This intervention includes investigation of disease clusters, administration of antiviral treatment to persons with confirmed or suspected pandemic influenza, and provision of drug prophylaxis to all likely exposed persons in the affected community. CDC will assist state health departments in these efforts, as needed.

Targeted chemoprophylaxis also requires intensive disease surveillance to ensure coverage of the entire affected area, effective communication with the affected community, and rapid distribution and administration of antivirals because they are most effective when provided within 48 hours of symptom onset or when used as post-exposure prophylaxis before onset of illness

2. Influenza hotlines and clinics

During the later phases of a Pandemic Alert, in a community experiencing a disease cluster, a combination of self-assessment and establishment of influenza hotlines may be effective in detecting potential influenza disease and conducting "community triage" to direct persons with symptoms to the appropriate site and level of care. This intervention includes asking all members of the affected community to monitor their symptoms in accordance with instructions from the state health department and CDC. For example, all members of the community might be asked to take their temperature (and the temperature of their household members) once or twice daily. Persons with temperatures above a certain level may be asked to either stay home and phone a designated influenza hotline for a medical referral, or proceed to a neighborhood influenza clinic established by local public health and healthcare authorities.

Healthcare workers at the clinic will determine whether the patient's symptoms are likely due to pandemic influenza, to a different contagious disease, or to a noncontagious condition. If a person is judged likely to be infected with pandemic influenza, they will be referred for isolation and care as needed.

The establishment of hotlines and influenza clinics requires preparation to identify sites and personnel and to facilitate the procurement and distribution of thermometers and other supplies. Clinic personnel should be prepared to keep records and report cases, as requested, by state health departments and CDC.

S8-IV. RECOMMENDATIONS FOR THE PANDEMIC PERIOD

During the Pandemic Period, control measures such as contact tracing and quarantine applied to individuals may have limited impact in decreasing influenza transmission. In addition, individual-level measures may no longer be feasible. During this stage, state and local health departments should consider measures that decrease social contact within groups or whole communities (e.g., self-shielding, cancellation of public events, snow days) and measures that individuals can take personally to decrease their risk of infection

Box 2 outlines measures that may be employed at different stages of a pandemic, as disease becomes more widespread. These begin with containment activities for individuals and move on, as needed, to community-based measures. Depending on the specific circumstances of an epidemic, these steps may not necessarily be taken in sequential order.

A. Containment measures for individuals

1. Patient isolation

As noted above, a patient with a suspected or confirmed case of pandemic influenza should be separated from persons who are well, using infection control measures described in **Supplement 4**. If a surge in patients overwhelms healthcare capacity or if home isolation is not feasible, health departments may need to use alternative facilities for isolation of influenza patients. Guidance on use of alternative facilities for isolation of influenza patients is provided in Appendix 7.

2. Management of contacts

Contact tracing, contact monitoring, and quarantine of close contacts may be effective only in special situations during the earliest stages of a pandemic. Because the usefulness and feasibility of these measures will be limited once the pandemic has started to spread, health authorities should consider community-based measures that reduce disease transmission by increasing social distance.

B. Community-based containment measures

If disease transmission in the community is significant and sustained, state and local public health authorities should consider implementing community-based containment measures. CDC will promote an active process of engagement and discussion to help states and localities decide what actions to take as the situation evolves. Community-based containment measures can be grouped into two broad categories: measures that affect groups of exposed or at-risk persons and measures that affect entire communities.

Table 1 lists quantifiable factors that may influence decisions on where and when to impose community-based containment measures. Social considerations—including levels of community cooperation and mobility—will also inform local decision-making.

1. Measures that affect groups of exposed or at-risk persons

Measures that affect groups of exposed or at-risk persons include:

- Quarantine of groups of exposed persons
- Containment measures that apply to use of specific sites or buildings

These measures should be considered when:

- There is limited disease transmission in the area.
- Most cases can be traced to contact with an earlier case or exposure to a known transmission setting (e.g., a school or workplace where a person has fallen ill).
- The intervention is likely to either significantly slow the spread of infection or to decrease the overall magnitude of an outbreak in the community.

a) Quarantine of groups of exposed persons

The purpose of quarantine is to reduce influenza transmission by separating exposed persons from others, monitoring exposed persons for symptoms, and providing medical care and infection control precautions as soon as symptoms are detected. Groups that might be quarantined include:

- Persons who might have been exposed to an influenza case
  - Via family members
  - At a public gathering
  - On an airplane or cruise ship or other closed conveyance (see also Supplement 9)
  - At their school or workplace
- Healthcare providers who work at a facility where influenza cases receive care

Group quarantine (like patient isolation) is optimally performed on a voluntary basis, in accordance with instructions of healthcare providers and health officials. However, many levels of government (local, state, federal) have the basic legal authority to compel mandatory isolation and quarantine of individuals and groups when necessary to protect the public's health (see below). Recommendations for quarantine and monitoring of quarantined persons in different situations (home quarantine, quarantine in a designated facility, working quarantine) are provided in Appendix 6.

b) Measures that apply to use of specific sites or buildings

Two ways of increasing social distance activity restrictions are to cancel events and close buildings or to restrict access to certain sites or buildings. These measures are sometimes called "focused measures to increase social distance." Depending on the situation, examples of cancellations and building closures might include:

- Cancellation of public events (concerts, sports events, movies, plays)
- Closure of recreational facilities (community swimming pools, youth clubs, gymnasiums)

2. Measures that affect communities

Measures that affect entire communities (including both exposed and non-exposed persons), include:

- Promotion of community-wide infection control measures (e.g., respiratory hygiene/cough etiquette)
- Snow days and self-shielding
- Closure of office buildings, shopping malls, schools, and public transportation (e.g., subways, buses; see **Supplement 9**)
- Widespread community quarantine (*cordon sanitaire*)

Measures that affect whole communities should be considered when:

- There is moderate to extensive disease transmission in the area.
- Many cases cannot be traced to contact with an earlier case or known exposure.
- Cases are increasing among contacts of influenza patients.
- There is a significant delay between the onset of symptoms and the isolation of cases because of the large number of ill persons.

As community outbreaks of pandemic influenza occur, community-wide infection control measures may decrease the overall magnitude of the outbreak (see Box 3). Community-based measures may also include school closures, snow days, and self-shielding.

a) Community-wide infection control measures

Throughout a pandemic, public health authorities will encourage all persons with signs and symptoms of a respiratory infection, regardless of presumed cause, to:

- Cover the nose/mouth when coughing or sneezing.
- Use tissues to contain respiratory secretions.
- Dispose of tissues in the nearest waste receptacle after use.
- Perform hand hygiene after contact with respiratory secretions and contaminated objects or materials.

Persons at high risk for complications of influenza will be advised to avoid public gatherings (e.g., movies, religious services, public meetings) when pandemic influenza is in the community. They should also avoid going to other public areas (e.g., food stores, pharmacies); the use of other persons for shopping or home delivery service is encouraged.

Disposable surgical-type masks are used by healthcare workers taking care of ill patients to prevent splashes and droplets of potentially infectious material (e.g., from coughs and sneezes) from reaching the mucous membranes of the healthcare worker's nose or mouth. The benefit of wearing masks by well persons in public settings has not been established and is not recommended as a public health control measure at this time. In contrast to healthcare workers who necessarily have close contact with ill patients, the general public should try to avoid close contact with ill individuals.

Nevertheless, persons may choose to wear a mask as part of individual protection strategies that include cough etiquette, hand hygiene, and avoiding public gatherings. Mask use may be most important for persons who are at high risk for complications of influenza and those who are unable to avoid close contact with others or must travel for essential reasons such as seeking medical care. Public education should be provided on how to use and dispose of masks appropriately. In addition, this education should emphasize that mask use is not a substitute for social distance or other personal protection measures (see also **Supplement 4**). Supply issues should be considered so that mask use in communities does not limit availability for healthcare settings where the importance and effectiveness of this use has been documented.

b) Snow days and self-shielding

Implementation of "snow days"—asking everyone to stay home—involves the entire community in a positive way, is acceptable to most people, and is relatively easy to implement. Snow days may be instituted for an initial 10-day period, with final decisions on duration based on an epidemiologic and social assessment of the situation. States and local authorities may wish to consider recommendations to the public for acquisition and storage of necessary provisions including type and quantity of supplies needed during snow days. Snow days can effectively reduce transmission without explicit activity restrictions (i.e., quarantine). Consideration should be given to personnel who maintain primary functions in the community (e.g., law enforcement personnel, transportation workers, utility workers [electricity, water, gas, telephone, sanitation]). Compliance with snow days might be enhanced by "self-shielding" behavior (i.e., many people may stay home even in the absence of an official snow day ["reverse quarantine"]).

c) Closure of office buildings, shopping malls, schools, and public transportation

Closure of office buildings, stores, schools, and public transportation systems may be feasible community containment measures during a pandemic. All of these have significant impact on the community and workforce, however, and careful consideration should be focused on their potential effectiveness, how they can most effectively be implemented, and how to maintain critical supplies and infrastructure while limiting community interaction. For example, when public transportation is cancelled, other modes of transportation must be provided for emergency medical services and medical evaluation.

Although data are limited, school closures may be effective in decreasing spread of influenza and reducing the overall magnitude of disease in a community. In addition, the risk of infection and illness among children is likely to be decreased, which would be particularly important if the pandemic strain causes significant morbidity and mortality among children. Children are known to be efficient transmitters of seasonal influenza and other respiratory illnesses. Anecdotal reports suggest that community influenza outbreaks may be limited by closing schools. Results of mathematical modeling also suggest a reduction of overall disease, especially when schools are closed early in the outbreak. During a Pandemic Period, parents should be encouraged to consider child care arrangements that do not result in large gatherings of children outside the school setting.

d) Widespread community quarantine (*cordon sanitaire*)

In extreme circumstances, public heath officials may consider the use of widespread or community-wide quarantine, which is the most stringent and restrictive containment measure. Strictly speaking, "widespread community quarantine" is a misnomer, since "quarantine" refers to separation of exposed persons only and (unlike snow days) usually allows provision of services and support to affected persons. Like snow days, widespread community quarantine involves asking everyone to stay home. It differs from snow days in two respects: 1) It may involve a legally enforceable action, and 2) it restricts travel into or out of an area circumscribed by a real or virtual "sanitary barrier" or "*cordon sanitaire*" except to authorized persons, such as public heath or healthcare workers.

Implementation of this measure during a pandemic is unlikely to prevent the introduction or spread of pandemic disease except in uncommon or unique circumstances (such as in a community able to be completely self-sufficient). In many cases, other less restrictive approaches such as snow days can be implemented to slow disease spread or decrease its magnitude in

a community. Because of this, *cordon sanitaire* is not recommended during a pandemic unless a community is in a setting where it is likely to be applied effectively and has planned with neighboring jurisdictions how such an approach would be implemented and maintained during a pandemic.

3. Scaling back community containment measures

The decision to discontinue community-level measures must balance the need to lift individual movement restrictions against community health and safety. Premature removal of containment strategies can increase the risk of additional transmission. Decisions should be based on evidence of improving local/regional control, such as:

- Consistent decrease in the number of confirmed cases
- Reduction in the number of probable and known cases
- Effective protective countermeasures are in place (e.g., high coverage with a pandemic influenza vaccine)

General recommendations are to withdraw the most stringent or disruptive measures first (e.g., widespread community quarantine, snow days, mass transit interruptions).

BOX 1. CONTAINMENT MEASURES: TERMS AND DEFINITIONS

Isolation is the separation and restriction and movement or activities of ill infected persons (patients) who have a contagious disease, for the purpose of preventing transmission to others.

Quarantine is the separation and restriction of movement or activities of persons who are not ill but who are believed to have been exposed to infection, for the purpose of preventing transmission of disease. Individuals may be quarantined at home or in designated facilities; healthcare providers and other response workers may be subject to quarantine when they are off duty.

Quarantine of close contacts refers to the quarantine of individuals exposed to patients with communicable diseases (e.g., family members, work or school mates, healthcare workers).

Quarantine of groups of exposed persons refers to quarantine of people who have been exposed to the same source of illness (e.g., a case of influenza at a public gathering, on an airline, train, or cruise ship, at a school or workplace or apartment complex, or at a recently visited store or office).

Widespread or community-wide quarantine refers to the closing of community borders or the erection of a real or virtual barrier around a geographic area (a cordon sanitaire) with prohibition of travel into or out of the area.

Self-shielding refers to self-imposed exclusion from infected persons or those perceived to be infected (e.g., by staying home from work or school during an epidemic).

Snow days are days on which offices, schools, transportation systems are closed or cancelled, as if there were a major snowstorm.

Influenza clinics are special facilities that may be established during a pandemic to provide rapid medical assessment of potentially infected persons. Ill persons would be encouraged to call influenza hotlines that provide advice on whether to stay home or seek help at an influenza clinic. Persons who come to an influenza clinic will be advised on whether they may be best served by hospital care or home care.

Individual-level containment measures include isolation of patients and management of their close contacts.

Focused measures to increase social distance (or decrease social contact) includes measures applied to groups rather than individuals or whole communities (e.g., quarantine of groups of exposed persons and measures that apply to the use of specific sites or buildings).

Containment measures that apply to use of specific sites or buildings include cancellation of public events (e.g., concerts, sports events, movies and plays), closure of office buildings, apartment complexes, or schools; and closure of subways or bus lines. These measures may also involve restricting entrance to buildings or other sites (e.g., requiring fever screening or use of face maskes before entry to schools, worksites, or airplanes).

Community-based measures to increase social distance include measures applied to whole neighborhoods, towns, or cities (e.g., snow days, establishment of fever clinics, and community-wide quarantine).

BOX 2. GRADED IMPLEMENTATION OF COMMUNITY CONTAINMENT MEASURES

Level of influenza activity	Response
No novel influenza strains of public health concern in global circulation	Preparedness planning
Limited novel influenza virus[2] transmission abroad; all local cases are either imported or have clear epidemiologic links to other cases	Quarantine of close contacts
Limited novel influenza virus transmission in the area, with either a small number of cases without clear epidemiologic links to other cases or with increased occurrence of influenza among their close contacts	Quarantine of close contacts
Sustained novel influenza virus transmission in the area, with a large number of cases without clear epidemiologic links to other cases; control measures aimed at individuals and groups appear to be effective	Focused measures to increase social distance;[3] consider community-based measures
Sustained novel influenza activity in the area, with a large number of cases in persons without an identifiable epidemiologic link at the time of initial evaluation; control measures are believed to be ineffective	Community-level measures to increase social distance; consider snow days and community-wide quarantine
Decreases in the number of new cases, unlinked (or "unexpected") cases, and generations of transmission	Quarantine of contacts
Transmission has been controlled or eliminated; no new cases reported	Active monitoring in high-risk populations; continue for 2-3 incubation periods after control or elimination of transmission.

[2] "Novel influenza viruses" include avian or animal influenza strains that can infect humans (like avian influenza A [H5N1]) and new or reemergent human viruses that cause cases or clusters of human disease.

[3] "Focused measures to increase social distance" include measures applied to groups rather than individuals or whole communities (e.g., quarantine of groups of exposed persons and measures that apply to the use of specific sites or buildings)

TABLE 1. THRESHOLD DETERMINANTS FOR THE USE OF COMMUNITY CONTAINMENT MEASURES

Data on cases and contacts—as well as on depletion of healthcare and public health resources over the course of a pandemic—can help state and local health authorities decide when to implement community-level containment measures. As part of preparedness planning, state and local health agencies and healthcare partners may estimate at what point in the pandemic—in terms of such variables as numbers of cases and numbers of unoccupied hospital beds—that more extensive measures may be imposed. During an actual pandemic, state and local departments may also evaluate social considerations, such as levels of community cooperation and mobility.

Potential parameters	Variable
Cases and contacts	Number of cases (absolute or estimated)
	Rate of incident cases
	Number of hospitalized cases
	Number and percentage of cases with no identified epidemiologic link
	Morbidity (including disease severity) and mortality
	Number of contacts under surveillance and/or quarantine
Healthcare resources	Hospital/facility bed capacity
	Staff resources
	Patient/staff ratio
	Number of ill or absent staff members
	Availability of specifically trained specialists and ancillary staff members
	Availability of ventilators
	Availability of other respiratory equipment
	Availability of personal protective equipment and other measures
	Availability of therapeutic medications (influenza and non-influenza specific)
Public health resources	Investigator to case and contact ratios
	Number of contacts under active surveillance
	Number of contacts under quarantine
	Ability to rapidly trace contacts (number of untraced/interviewed contacts)
	Ability to implement and monitor quarantine (staff member to contact ratio)
	Ability to provide essential services (food, water, etc.)
Community cooperation, mobility, and compliance	Degree of compliance with voluntary individual isolation
	Degree of compliance with active surveillance and voluntary individual quarantine
	Degree of movement out of the community
	Degree of compliance with community-containment measures

APPENDIX 1. INTERVENTIONS FOR COMMUNITY CONTAINMENT

Contacts of pandemic influenza patients can be managed by use of a range of interventions, all of which are designed to facilitate early recognition of illness in persons at greatest risk of becoming infected and thereby prevent transmission to others. Whereas many of these interventions are applied individually to persons identified as contacts of a person with possible or known influenza disease, others are applied to larger groups of persons, or communities, that share a similar risk of exposure. Measures applied to individuals may not be feasible during the Pandemic Period, when quarantining individuals and tracing close contacts may not be possible. The range of interventions includes the following:

Passive Monitoring

Definition	The contact is asked to perform self-assessment at least twice daily and to contact authorities immediately if respiratory symptoms and/or fever occur.
Application	Situations in which 1) the risk of exposure and subsequent development of disease is low, and 2) the risk to others if recognition of disease is delayed is also low
Benefits	Requires minimal resources Places few constraints on individual movement
Challenges	Relies on self-reporting Affected persons may not perform an adequate self-assessment
Resources Required	Supplies (thermometer; symptom log; written instructions) Hotline to notify authorities about symptoms or needs Staff to receive telephone reports and provide in-person evaluation and care Plans and procedures for rapid isolation of persons who develop symptoms
Partners	Household members
Forms/Templates	Symptom logs Instructions for patients and healthcare workers

Active Monitoring without Explicit Activity Restrictions

Definition	A healthcare or public health worker evaluates the contact on a regular (at least daily) basis by phone and/or in person for signs and symptoms suggestive of influenza
Application	Situations in which 1) the risk of exposure to and subsequent development of disease is moderate to high, 2) resources permit close observation of individuals, and 3) the risk of delayed recognition of symptoms is low to moderate
Benefits	Places few constraints on individual liberties
Challenges	Requires adequate staffing Requires a system to track information and to verify monitoring and appropriate actions based on findings
Resources Required	Trained staff to provide in-person and/or telephone evaluations Plans and procedures for rapid isolation of persons who develop symptoms Contingency plans for managing noncompliant persons Hotline to notify authorities about symptoms or needs

Partners	Professional and lay healthcare workers to perform evaluations on behalf of the health department Possible need for law enforcement to assist with management of noncompliant persons
Forms/Templates	Checklist for assessment of active monitoring Template for recording results of clinical evaluation

Active Monitoring with Activity Restrictions (Quarantine)

Definition	The contact remains separated from others for a specified period (up to 10 days after potential exposure), during which s/he is assessed on a regular basis (in person at least once daily) for signs and symptoms of influenza disease. Persons with fever, respiratory, or other early influenza symptoms require immediate evaluation by a trained healthcare provider. Restrictions may be voluntary or legally mandated; confinement may be at home or in an appropriate facility. No specific precautions are required for those sharing the household with a person in quarantine as long as the person remains asymptomatic. Because onset of symptoms may be insidious, it may be prudent to minimize interactions with household members during the period of quarantine, if feasible
Application	Situations in which the risk of exposure and subsequent development of disease is high and the risk of delayed recognition of symptoms is moderate
Benefits	Reduces risk of spread from persons with subacute or subclinical presentations or from delayed recognition of symptoms
Challenges	May infringe on personal movement May lead to a feeling of isolation from family and friends May lead to loss of income or employment Requires plans/protocols for provision of essential services Requires plan for provision of mental health support Risk of noncompliance, particularly as duration increases May require enforcement for noncompliance
Resources Required	Staff for monitoring and evaluation Appropriate facility if home setting is unavailable or inadequate Staff, funding, and goods for provision of essential services Hotline for notification of symptoms or personal needs Mechanisms to communicate with family members outside the household or facility Mental health and social support services Delivery systems for food and other essential supplies
Partners	Professional and lay healthcare workers to perform assessments on behalf of the health department Community volunteers/workers to assist with provision of essential services Potential need for law enforcement to assist with noncompliant persons

Forms/Templates	Checklist for active monitoring Template for recording results of clinical evaluation Checklist and guidelines for evaluation of homes for quarantine Checklist and guidelines for evaluation of community-based sites for quarantine Guidelines for monitoring compliance with home quarantine Guidelines for monitoring compliance with quarantine in community-based facilities Forms for recording compliance with quarantine
Examples	Home quarantine (voluntary or mandatory) Facility quarantine (voluntary or mandatory)

Working Quarantine

Definition	Employees are permitted to work but must observe activity restrictions while off duty. Monitoring for influenza-like illness before reporting for work is usually required. This may change based on the clinical presentation of the pandemic strain. Use of appropriate PPE while at work is required (see **Supplement 4**)
Application	Persons for whom activity restrictions (home or facility quarantine) are indicated but who provide essential services (e.g., healthcare workers)
Benefits	Reduces risk of community spread from high-risk contacts while minimizing adverse impact of activity restrictions on provision of essential services Clinical monitoring at work reduces the staff required for active monitoring at the quarantine site
Challenges	Need for close and consistent pre-shift monitoring at the work site to prevent inadvertent exposures May require means of transporting persons to and from work site to minimize interactions; persons in working quarantine should wear appropriate PPE during transport. (See **Supplement 4**) Must maintain close cooperation and communication between work site and local health authorities Need to provide mental health services to address concerns about isolation from family and friends
Resources Required	Appropriate facility for off-duty quarantine if home is unavailable or inadequate Staff, funding, and goods for provision of essential services Personal protective equipment (see **Supplement 4**) Hotline for notification of symptoms and personal needs System to track results of work-site monitoring and location(s) of off-duty quarantine Mental health, psychological, and behavioral support services, especially if work includes care of influenza patients
Partners	Work-site administrators and infection control personnel Community volunteers/workers Staff/volunteers to assist with transportation to and from work Mental health professionals Potential need for law enforcement to assist with noncompliant persons

Forms/Templates	Guidelines and instructions for persons in working quarantine Instructions for supervisors of persons in working quarantine Checklist to evaluate homes for quarantine Guidelines for monitoring compliance Checklist for active monitoring at work site Template for recording results of clinical evaluation Forms for recording compliance

Focused Measures to Increase Social Distance

Definition	Intervention applied to specific groups, designed to reduce interactions and thereby transmission risk within the group. When focused, the intervention is applied to groups or persons identified in specific sites or buildings, most but not necessarily all of whom are at risk of exposure to influenza.
Examples	Quarantine of groups of exposed persons Cancellation of public events Closure of office buildings, schools, and/or shopping malls; closure of public transportation such as subways or bus lines
Application	Groups or settings where transmission is believed to have occurred, where the linkages between cases is unclear at the time of evaluation, and where restrictions placed only on persons known to have been exposed is considered insufficient to prevent further transmission
Benefits	Applied broadly, reduces the requirement for urgent evaluation of large numbers of potential contacts to determine indications for activity restrictions May enable reductions in transmission among groups of persons without explicit activity restrictions (quarantine)
Challenges	May be difficult to solicit cooperation, particularly if popular buildings are closed or popular events are cancelled Requires excellent communication mechanisms to notify affected persons of details and rationale May need to provide replacement for affected activities (e.g., school, essential services) Generally relies on passive monitoring
Resources Required	Systems to communicate relevant messages May require enforcement, particularly if closure of buildings or gathering places is necessary Requires resources for passive monitoring Hotlines to report symptoms and obtain follow-up instructions Transportation for medical evaluation, with appropriate infection control precautions
Partners	News media and communication outlets Law enforcement Community groups
Forms/Templates	Messages for affected persons Messages for employers of affected persons Messages for persons supplying essential services

Community-Wide Measures to Increase Social Distance

Definition	Intervention applied to an entire community or region, designed to reduce personal interactions and thereby transmission risk. The prototypical example is implementation of a "snow day," in which offices, schools, and transportation systems are cancelled as for a major snowstorm.
Examples	Snow days
Application	All members of a community in which 1) extensive transmission of influenza is occurring, 2) a significant number of cases lack clearly identifiable epidemiologic links at the time of evaluation, and 3) restrictions on persons known to have been exposed are considered insufficient to prevent further spread
Benefits	Reduces need for urgent evaluation of large numbers of potential contacts to determine indications for activity restrictions May enable reductions in transmission among groups without explicit activity restrictions (quarantine) "Snow days" are familiar concepts and thus are easy to implement on short notice
Challenges	May be difficult to solicit cooperation Requires excellent communication mechanisms to notify affected persons of details and rationale May need to provide replacement for affected activities (e.g., school, essential services) May need to address mental health and financial support issues When an entire community is involved, requires cooperation with neighboring jurisdictions that may not be using a similar intervention, particularly in situations where persons live in one city and work in another and only one locale is affected by the intervention Generally relies on passive monitoring Social and economic impact of public transportation closures
Resources Required	Communication outlets Enforcement Resources for passive monitoring Hotlines and other communication systems to report symptoms and obtain follow-up instructions
Partners	News media and other communication outlets Law enforcement and transportation officials to enforce restrictions (e.g., closure of bridges, roads, or mass transit systems) and plan for provision of critical supplies and infrastructure
Forms/Templates	Messages for affected persons Messages for employers of affected persons Messages for persons supplying essential services

Widespread Community Quarantine, Including Cordon Sanitaire

Definition	Legally enforceable action that restricts movement into or out of the area of quarantine of a large group of people or community; designed to reduce the likelihood of transmission of influenza among persons in and to persons outside the affected area. When applied to all inhabitants of an area (typically a community or neighborhood), the intervention is referred to as *cordon sanitaire* (sanitary barrier).

Application	All members of a group in which 1) extensive transmission is occurring, 2) a significant number of cases lack identifiable epidemiologic links at the time of evaluation, and 3) restrictions placed on persons known to have been exposed are considered insufficient to prevent further spread. Widespread quarantine is unlikely to be necessary because other less restrictive measures (e.g., snow days) may be equally effective.
Benefits	Reduces need for urgent evaluation of large numbers of potential contacts to determine indications for activity restrictions
Challenges	Controversial because of the degree that individual movement is restricted Difficult to solicit cooperation for extended periods, particularly if the rationale is not readily apparent or was not clearly explained Requires excellent communication mechanisms to inform affected persons and to maintain public confidence in the appropriateness of the chosen course of action Need to ensure continuation of essential services Need to provide financial support and mental health support services for the affected population When an entire community is involved, requires cooperation with neighboring jurisdictions that may not be using a similar intervention, particularly in situations where persons live in one city and work in another and only one locality is affected by the intervention Need to provide mechanisms for isolating symptomatic persons with minimal delay
Resources Required	Systems to communicate relevant messages Enforcement to maintain security at borders Transportation for persons requiring medical evaluation, with appropriate infection control precautions Staff and supplies to maintain access to and availability of essential services and goods, including food, water, medicine, medical care, and utilities Psychological support staff Plan to divert flow of critical infrastructure supplies and materials that normally transit through quarantined area
Partners	News media and other mass communication outlets Public and private groups, industries, and officials to coordinate supply and provision of essential services to affected area Law enforcement to maintain security at borders and to enforce movement restrictions Transportation industry
Forms/Templates	Messages for affected persons Messages for employers of affected persons Messages for persons supplying essential services
Examples	Quarantine (*cordon sanitaire*) of a city or town Quarantine of occupants of a housing complex or office building

APPENDIX 2. PREPAREDNESS CHECKLIST FOR COMMUNITY CONTAINMENT MEASURES

General

- ❑ Establish an incident command structure that can be used for influenza response.
- ❑ Establish a legal preparedness plan.
- ❑ Establish relationships with partners, such as law enforcement, first responders, healthcare facilities, mental health professionals, local businesses, and the legal community.
- ❑ Plan to monitor and assess factors that will determine the types and levels of response, including the epidemiologic profile of the outbreak, available local resources, and level of public acceptance and participation.
- ❑ Develop communication strategies for the public, government decision-makers, healthcare and emergency response workers, mental health professionals, and the law enforcement community.
- ❑ Invite key partners to participate in pandemic influenza containment exercises and drills.

Management of cases and contacts (including quarantine)

- ❑ Develop protocols, tools, and databases for:
  - Case surveillance
  - Clinical evaluation and management
  - Contact tracing, monitoring, and management
  - Reporting criteria
- ❑ Develop standards and tools for home and non-hospital isolation and quarantine.
- ❑ Establish supplies for non-hospital management of cases and contacts.
- ❑ Establish a telecommunications plan for "hotlines" or other services for:
  - Case and contact monitoring and response
  - Fever triage
  - Public information
  - Provider information
- ❑ Plan to ensure provision of essential services and supplies to persons in isolation and quarantine, keeping in mind the special needs of children. Services and supplies include:
  - Food and water
  - Shelter
  - Medicines and medical consultations
  - Mental health and psychological support services
  - Other supportive services (e.g., day care or elder care)
  - Transportation to medical treatment, if required
- ❑ Plan to address issues of financial support, job security, and prevention of stigmatization.
- ❑ Establish procedures for medical evaluation and isolation of quarantined persons who exhibit signs of illness.

- ❑ Develop protocols for monitoring and enforcing quarantine measures, such as:
  - Protocols for follow-up of persons who cannot be reached by telephone. These may include a threshold period for nonresponsiveness that should trigger a home visit or other means to locate the person. Partnerships with law enforcement and other community-based resources will be helpful in tracing the whereabouts of persons who have violated restrictions.
  - Protocols for monitoring persons who cannot or will not comply with voluntary home quarantine. These may include:
    - Issuing official, legally binding quarantine orders
    - Posting a guard outside the home
    - Using electronic forms of monitoring
    - Using guarded facilities
  - Protocols for using checkpoints to restrict travel between neighborhoods.

Temporary emergency facilities for patient isolation quarantine, and assessment of patients with fever (see Appendix 7 for a list of facility characteristics)

- ❑ Identify appropriate community-based facilities for isolation of patients who have no substantial healthcare requirements.
- ❑ Develop policies related to use of these facilities.
- ❑ Identify facilities for persons for whom home isolation is indicated but who do not have access to an appropriate home setting, such as travelers and homeless populations.
- ❑ Ensure that required procedures for assessment of potential isolation or quarantine sites are available and up to date.
- ❑ Identify potential quarantine facilities and prepare contingency plans for staffing and equipping them.
- ❑ Identify potential sites for fever clinics and prepare contingency plans for staffing and equipping them, including the ability to dispense antiviral drugs to identified cases in the priority groups.

Community containment measures

- ❑ Ensure that legal authorities and procedures are in place to implement the various levels of movement restrictions as necessary.
- ❑ **Establish procedures for medical evaluation and isolation of quarantined persons who exhibit signs of illness.** (Additional information on medical evaluation is provided in **Supplement 5.**)
- ❑ **Develop tools and mechanisms to prevent stigmatization and provide mental health services to persons in isolation or quarantine.**
- ❑ Identify key partners and personnel for the implementation of movement restrictions, including quarantine, and the provision of essential services and supplies:
  - Law enforcement
  - First responders
  - Other government service workers
  - Utilities
  - Transportation industry
  - Local businesses
  - Schools and school boards

Establish procedures for delivering medical care, food, and services to persons in isolation or quarantine. Examples of services that will require the help of non-traditional partners include:

- ❑ Training for responders and healthcare workers, as necessary, in use of personal protective equipment
- ❑ Plans for the mobilization and deployment of public health and other community-service personnel

General

- ❑ Establish an incident command structure that can be used for influenza response.
- ❑ Establish a legal preparedness plan.
- ❑ Establish relationships with partners, such as law enforcement, first responders, healthcare facilities, mental health professionals, and the legal community.
- ❑ Plan to monitor and assess factors that will determine the types and levels of response, including the epidemiologic profile of the outbreak, available local resources, and level of public acceptance and participation.
- ❑ Develop communication strategies for the public government decision-makers, healthcare and emergency response workers, mental health professionals, and the law enforcement community. These strategies should consider privacy concerns.
- ❑ Invite key partners to participate in pandemic influenza containment exercises and drills.

Management of cases and contacts (including quarantine)

- ❑ Develop protocols, tools, and databases for management of cases and contacts, considering account security and privacy concerns. These may include protocols for:
  - Case surveillance
  - Clinical evaluation and management
  - Contact tracing, monitoring, and management
  - Reporting criteria
- ❑ Develop standards and tools for home and non-hospital isolation and quarantine.
- ❑ Establish supplies for non-hospital management of cases and contacts.
- ❑ Establish a telecommunications plan for "hotlines" or other services for case and contact monitoring and response
  - Fever triage
  - Public information
  - Provider information
- ❑ Plan to ensure provision of essential services and supplies to persons in isolation and quarantine, including:
  - Food and water
  - Shelter
  - Medicines and medical consultations
  - Mental health and psychological support services
  - Other supportive services (e.g., day care or elder care).
  - Transportation to medical treatment, if required
- ❑ Plan to address issues of financial support, job security, privacy concerns and prevention of stigmatization.

APPENDIX 3. RECENT EXPERIENCE WITH QUARANTINE: THE 2003 SARS OUTBREAK

Large-scale quarantine strategies were implemented during the 2003 SARS outbreak in several severely affected countries. Strategies included quarantine of close contacts in healthcare and household settings, work and school contacts, travelers arriving from other SARS-affected areas, and in some cases, of entire apartment complexes or areas of a city. Other strategies used to control and prevent SARS transmission in these countries included 1) requiring fever screening before entry to schools, work sites, and other public buildings; 2) requiring use of face masks in certain settings, such as public transportation systems; 3) implementing population-wide temperature monitoring and SARS fever hotlines and referral services; and 4) implementing community-level disinfection strategies.

The impact and effectiveness of individual isolation and quarantine measures and community- and population-level interventions undertaken to contain the SARS epidemic globally are not yet fully understood, but some important generalizations can be made. Overall, strategies associated with timely and successful control of local outbreaks were characterized by rapid and aggressive use of case and contact identification and community containment strategies.

Other lessons learned from this modern experience with community containment include the following:

- Strict infection control measures were needed for isolation of SARS patients; these may be difficult to implement in home and community settings.
- Community control measures such as cancellation of public events and other "snow day" measures may have reduced the risk of exposure to SARS at the population level by limiting social interactions.
- Although quarantine of individual contacts was an integral part of SARS control in most settings, quarantine of large groups was used only in selected settings where transmission was extensive.
- To be effective, quarantine did not have to be mandatory and compliance did not have to be 100%; voluntary compliance with quarantine requests was >90% in most settings.
- A variety of quarantine strategies (e.g., home quarantine, working quarantine) were used, depending on specific needs.
- Isolation and quarantine raised legal, social, financial, psychological, and logistical challenges (e.g., financial support, provision of services, prevention of stigmatization and discrimination) that should be anticipated and addressed in the future. Meeting the social, financial, and psychological needs of persons in isolation and quarantine and their contacts was key to the successful application of containment measures.
- Effective implementation of quarantine required a clear understanding of the roles and legal authorities of local, state, and federal public health officials.
- Effective implementation of quarantine required identification and engagement of appropriate traditional and non-traditional partners (e.g., law enforcement) in coordinated planning and response.
- The financial, social, and psychological impact of quarantine measures is substantial; preparedness planning should include measures to reduce this impact.
- Obtaining and maintaining public trust are key to successful implementation of these measures; clear messages about the criteria, justification, role, and duration of quarantine and ways in which persons will be supported during the quarantine period will help generate public trust.

APPENDIX 4. PRINCIPLES OF MODERN QUARANTINE

The goal of quarantine is to protect the public by separating those exposed to a dangerous communicable disease from the general population. It represents collective action for the common good that is predicated on aiding individuals who are already infected or exposed and protecting others from inadvertent exposure. Principles of modern quarantine[4] include:

Principle 1. Modern quarantine is used when:

- A person or a well defined group of people has been exposed to a highly dangerous and highly contagious disease
- Resources are available to care for quarantined people
- Resources are available to implement and maintain the quarantine and deliver essential interventions

Principle 2. Modern quarantine encompasses a range of disease-containment strategies, Including:

- Short-term, voluntary home-curfew
- Restrictions on the assembly of groups of people (e.g., school events)
- Cancellation of public events
- Suspension of public gatherings and closings of public places (e.g., theaters)
- Restrictions on travel (air, rail, water, motor vehicle, pedestrian)
- Closure of mass transit systems
- Snow days
- "Cordon sanitaire" (a guarded barrier restricting passage in and out of an area)

Principle 3. Modern quarantine is used in combination with other interventions and public health tools, including:

- Enhanced disease surveillance and symptom monitoring
- Rapid diagnosis and treatment for those who fall ill
- Preventive interventions for quarantined individuals, including vaccination or prophylactic treatment, depending on the disease

Principle 4. Quarantined individuals will be sheltered, fed, and cared for under the supervision of trained healthcare professionals. They will also be among the first to receive all available medical interventions to prevent and control disease, including:

- Vaccination (e.g., in the case of smallpox)
- Antibiotics (e.g., in the case of plague)
- Early and rapid diagnostic testing and symptom monitoring
- Early treatment if symptoms appear

Quarantined people may be cared for at home, in a designated emergency facility, or in a specialized hospital, depending on the disease and the available resources.

[4] These principles apply to the use of quarantine as a control measure against a wide variety of infectious diseases.

Principle 5. Modern quarantine lasts only as long as necessary to protect the public by providing public health interventions (e.g., immunization or drug treatment, as required) and ensuring that quarantined persons do not become ill or infect others.

Principle 6. Modern quarantine does not have to be absolute to be effective. Modeling exercises suggest that partial quarantine can be effective in slowing the rate of smallpox spread, especially when combined with vaccination. The goal is to reduce the reproductive rate (the number of secondary cases from an index case) to < 1 to extinguish an epidemic.

Principle 7. Modern quarantine is more likely to involve limited numbers of exposed persons in small area, than to involve large numbers of persons in whole neighborhoods or cities. The small areas may be thought of as "boxes" or "concentric circles" drawn around individual disease cases. Logistical issues will vary in each case, depending on the size and location of the boxes.

Examples of "boxes" include:

- People on an airplane or cruise ship on which a passenger is ill with a suspected quarantinable disease
- People who have contact with a contagion-infected person whose source of disease exposure is unknown

Principle 8. Implementation of modern quarantine requires a clear understanding of public health roles at the local, state, and federal levels, based on well understood legal authorities at each level.

Principle 9. Implementation of modern quarantine requires coordinated preparedness planning by many public and private response partners, including agencies and groups involved in public health, healthcare, transportation, emergency response, law enforcement, and security.

Principle 10. Implementation of modern quarantine requires the trust and participation of the general public, who must be informed about the dangers of quarantinable diseases before an outbreak occurs, as well as during an actual event.

APPENDIX 5. FREQUENTLY ASKED QUESTIONS ABOUT QUARANTINE

If an influenza pandemic occurs, will my community be quarantined?

Community-wide quarantine is only one of a spectrum of actions that may be considered during an influenza pandemic in the United States. Although rapid control is likely to require bold and swift action, measures that are less drastic than legally enforced quarantine may suffice, depending on the epidemiologic characteristics of the pandemic. For example, active monitoring without activity restrictions may be adequate when most cases are either imported or have clear epidemiologic linkages at the time of initial evaluation. When the epidemiology of the outbreak indicates a need for stronger measures, jurisdictions can adopt a voluntary quarantine approach and reserve compulsory measures for only extreme situations. When an outbreak progresses to include large numbers of cases for which no epidemiologic linkages can be identified, community-level interventions may become necessary. Even at this stage, however, measures designed to increase social distance, such as snow days, may be preferred alternatives to quarantine. Wider use of quarantine is generally reserved for situations in which all other control measures are believed to be ineffective.

The choice of containment measures requires frequent and ongoing assessment of an outbreak and evaluation of the effectiveness of existing control measures. Officials must be prepared to make decisions based on limited information and then modify those decisions as additional information becomes available.

Does the effectiveness of containment measures require 100% compliance?

No. Containment measures, including quarantine, are effective even if compliance is less than 100%. Although health officials should strive for high compliance, even partial or "leaky" quarantine can reduce transmission. Therefore, strict enforcement is not always needed; in most cases, jurisdictions can rely on voluntary cooperation. The incremental benefit of quarantine approaches a maximum at a compliance rate of approximately 90%, with little additional benefit from higher rates of compliance. Therefore, containment measures can be important components of the response to a communicable disease outbreak even when compliance is not 100%.

Does "quarantine" always mean using a legal order to restrict someone's activity?

No. The term "quarantine" is often defined narrowly to refer to the legally mandated separation of well persons who have been exposed to a communicable disease from those who have not been exposed. Although the precise legal definition of quarantine may differ from jurisdiction to jurisdiction, when used clinically or programmatically, quarantine may be defined more broadly to include all interventions, both mandatory and voluntary, that restrict the activities of persons exposed to a communicable disease. Therefore, whenever an exposed person is placed under a regimen of monitoring that includes an activity restriction, even when those restrictions are voluntary, the person is said to be under quarantine.

Must quarantine be mandatory to be effective?

Although the federal government and nearly all states have the basic legal authority to place persons exposed to certain communicable diseases under quarantine and enforce the required restrictions on activity, use of this authority may not always be necessary or practical. Previous experiences with the use of quarantine, including those during the 2003 SARS outbreak, suggest that the majority of persons comply voluntarily with requests from health authorities to remain in quarantine and observe the recommended activity restrictions. In the event voluntary measures are not successful, it may be necessary to implement mandatory containment measures.

Does being placed in quarantine increase a person's risk for acquiring disease?

One of the fundamental principles of modern quarantine is that persons in quarantine are to be closely monitored so that those who become ill are efficiently separated from those who are well. A second principle is that persons in quarantine should be among the very first to receive any available disease-prevention interventions. Adherence to these two principles of modern quarantine should prevent an increase in risk for acquiring disease while in quarantine.

Is quarantine really necessary if everyone who develops symptoms is rapidly placed in isolation?

Although theoretically true, it would be unrealistic to believe that even the most efficient system for initiation of isolation will minimize delays to the extent required to prevent transmission. Among the factors contributing to delays in recognition of symptoms are the insidious nature of disease onset and denial that symptoms have developed. Early in the 2003 SARS outbreak in Singapore, the average delay from onset of symptoms to initiation of isolation was 7 days. Officials were able to reduce this delay only to 3 days, even with an aggressive public awareness campaign on the importance of symptom recognition and isolation.

Quarantine helps to reduce transmission associated with delays in isolation in two ways. First, quarantine enables health officials to quickly locate symptomatic persons who should be placed in isolation. Second, although quarantine locations may not be as efficient as isolation facilities in preventing transmission, quarantine reduces the number of persons who might be exposed while awaiting transfer to an isolation facility. If quarantine was not used, symptomatic and infectious persons could move about freely in public places, potentially exposing large numbers of additional persons and thereby fueling the outbreak.

Is quarantine useful only for diseases that are spread by the airborne route?

No. Quarantine simply refers to the separation and restriction of activity of persons exposed to a communicable disease who are not ill. It is designed to minimize interactions between those exposed to a disease and those not yet exposed. As such, quarantine can be used for any disease that is spread from person to person. In practice, however, because of the activity restrictions associated with quarantine, the intervention is generally reserved for diseases like SARS or pandemic influenza that are easily and rapidly spread from person to person. The indication for quarantine for diseases purely transmitted by the airborne route is clear. However, this tool can also be useful where transmission can occur through close personal contact with secretions or objects contaminated by an ill person. Smallpox is an excellent example of a disease where quarantine can be effective in controlling spread although transmission may occur by means other than the airborne route.

Will the public accept the use of quarantine?

Yes. The negative connotations associated with quarantine likely stem from its misuse or abuse in the past. Although inappropriate use of quarantine, either voluntary or mandatory, would not and should not be accepted by the public, efforts should be made to gain public acceptance when use of this measure is indicated. Experiences with the use of quarantine during the SARS outbreaks of 2003 suggest that public acceptance of quarantine may be greater than previously thought. For example, during the 2003 SARS outbreak in Canada, almost all persons asked to observe quarantine restrictions did so willingly, with only a small number requiring a legal order to gain cooperation. In all cases, cooperation and acceptance was achieved through clear and comprehensive communication with the public about the rationale for use of quarantine.

APPENDIX 6. RECOMMENDATIONS FOR QUARANTINE

(Note: Recommendations on patient isolation are provided in **Supplement 3.**)

General considerations

- Monitor each quarantined person daily, or more frequently if feasible, for fever, respiratory symptoms, and other symptoms of early influenza disease.
- Monitor compliance with quarantine through daily visits or telephone calls.
- Provide a hotline number for quarantined persons to call if they develop symptoms or have other immediate needs.
- If a quarantined person develops symptoms suggestive of influenza, arrangements should be in place for separating that person from others in quarantine and ensuring immediate medical evaluation.
- Provide persons in quarantine with all needed support services, including 1) psychological support, 2) food and water, 3) household and medical supplies, and 4) care for family members who are not in quarantine. Financial issues, such as medical leave, may also need to be considered.
- Collect data related to quarantine activities to guide ongoing decision-making including information on each person quarantined:
  - Relationship to the case-patient
  - Nature and time of exposure
  - Whether the contact was vaccinated or on antiviral prophylaxis or using PPE
  - Underlying medical conditions
  - Number of days in quarantine
  - Symptom log
  - Basic demographics
  - Compliance with quarantine

Based on current available data, the recommended duration of quarantine for influenza is generally **10 days** from the time of exposure. (This period may be adjusted based on available information during a pandemic.) At the end of the designated quarantine period, contacts should have a final assessment for fever and respiratory symptoms. Persons without fever or respiratory symptoms may return to normal activities.

Home quarantine

Whenever possible, contacts should be quarantined at home. Home quarantine requires the fewest additional resources, although arrangements must still be made for monitoring patients, reporting symptoms, transporting patients for medical evaluation if necessary, and providing essential supplies and services. Home quarantine is most suitable for contacts with a home environment that can meet their basic needs and in which unexposed household members can be protected from exposure. Other considerations include:

- Persons in home quarantine must be able to monitor their own symptoms (or have them monitored by a caregiver).
- The person's home should be evaluated for suitability before being used for quarantine, using a questionnaire administered to the quarantined person or the caregiver. Additional guidance on use of a residence for quarantine is provided in Appendix 7.

- Quarantined persons should minimize interactions with other household members to prevent exposure during the interval between the development and recognition of symptoms. Precautions may include 1) sleeping and eating in a separate room, 2) using a separate bathroom, and 3) appropriate use of personal protective equipment (see **Supplement 4**).
- Persons in quarantine may be assessed for symptoms by either active or passive monitoring. Active monitoring of contacts in quarantine may overcome delays resulting from the insidious onset of symptoms or denial among those in quarantine.
- Household members may go to school, work, etc., without restrictions unless the quarantined person develops symptoms. If the quarantined person develops symptoms, household members should remain at home in a room separate from the symptomatic person and await additional instructions from health authorities.
- Household members can provide valuable support to quarantined persons by helping them feel less isolated and ensuring that essential needs are met.
- Immediate and ongoing psychological support services should be provided to minimize psychological distress.
- Quarantined persons should be able to maintain regular communication with their loved ones and healthcare providers.

Quarantine in designated facilities

In some cases, affected persons may not have access to an appropriate home environment for quarantine. Examples include travelers; persons living in dormitories, homeless shelters, or other group facilities; and persons whose homes do not meet the minimum requirements for quarantine. In other instances, contacts may have an appropriate home environment but may not wish to put family members at risk. In these situations, health officials should identify an appropriate community-based quarantine facility. Monitoring of quarantined persons may be either passive or active, although active monitoring may be more appropriate in a facility setting. Facilities designated for quarantine of persons who cannot or choose not to be quarantined at home should meet the same criteria listed for home quarantine. Evaluation of potential sites for facility-based quarantine is an important part of preparedness planning (see Appendix 7).

Working quarantine

This type of quarantine applies to healthcare workers or other essential personnel who are at occupational risk of influenza infection. These groups may be subject to quarantine either at home or in a designated facility during off-duty hours. When off duty, contacts on working quarantine should be managed in the same way as persons in quarantine at home or in a designated facility. Local officials should:

- Monitor persons in working quarantine for symptoms during work shifts
- Promptly evaluate anyone who develops symptoms
- Provide transportation to and from work, if needed
- Develop mechanisms for immediate and ongoing psychological support

At the end of the designated quarantine period, contacts should receive physical (fever and respiratory symptoms) and psychological health assessments. Persons without fever or respiratory symptoms may return to normal activities. Persons who exhibit psychological distress should be referred to mental health professionals for additional support services.

APPENDIX 7. EVALUATION OF HOMES AND FACILITIES FOR ISOLATION AND QUARANTINE

ISOLATION FACILITIES

Home isolation

Ideally, persons who meet the criteria for a case of pandemic influenza and who do not require hospitalization for medical reasons should be isolated in their homes. The home environment is less disruptive to the patient's routine than isolation in a hospital or other community setting.

If feasible—especially during the earliest stages of a pandemic—a home being considered as an isolation setting should be evaluated by an appropriate authority, which could be the patient's physician, health department official, or other appropriate person to verify its suitability. The assessment should center on the following minimum standards for home isolation of an influenza patient:

Infrastructure

- Functioning telephone
- Electricity
- Heating, ventilation, and air conditioning (HVAC)
- Potable water
- Bathroom with commode and sink
- Waste and sewage disposal (septic tank, community sewage line)

Accommodations

- Ability to provide a separate bedroom for the influenza patient
- Accessible bathroom in the residence; if multiple bathrooms are available, one bathroom designated for use by the influenza patient

Resources for patient care and support

- Primary caregiver who will remain in the residence and who is not at high risk for complications from influenza disease
- Meal preparation
- Laundry
- Banking
- Essential shopping
- Social diversion (e.g., television, radio, Internet access, reading materials)
- Masks, tissues, hand hygiene products, and information on infection control procedures
- Educational material on proper waste disposal

Isolation in a community-based facility

When persons requiring isolation cannot be accommodated either at home or in a healthcare facility, a community-based isolation facility will be required. The availability of a community-based facility will be particularly important during a large outbreak (See also http://www.ahrq.gov/research/altsites.htm).

Much of the work in identifying and evaluating potential sites for isolation should be conducted in advance of an outbreak as part of preparedness planning. Each jurisdiction should assemble a team (including infection control specialists, public health authorities, engineers, sanitation experts, and mental health specialists) to identify appropriate locations and resources for community influenza isolation facilities, establish procedures for activating them, and coordinate activities related to patient management. The team should consider the use of both existing and temporary structures. Options for existing structures include community health centers, nursing homes, apartments, schools, dormitories, and hotels. Options for temporary structures include trailers, barracks, and tents. Considerations include:

Basic infrastructure requirements

- Meets all local code requirements for a public facility
- Functioning telephone system
- Electricity
- Heating, ventilating, and air conditioning (HVAC)
- Potable water
- Bathroom with commode and sink
- Waste and sewage disposal (septic tank, community sewage line)
- Multiple rooms for housing ill patients (individual rooms are preferred)

Access considerations

- Proximity to hospital
- Parking space
- Ease of access for delivery of food and medical and other supplies
- Handicap accessibility
- Basic security

Space requirements

- Administrative offices
- Offices/areas for clinical staff
- Holding area for contaminated waste and laundry
- Laundry facilities (on- or off-site)
- Meal preparation (on- or off-site)

Social support resources

- Television and radio
- Reading materials

To determine priorities among available facilities, consider these features:

- Separate rooms for patients or areas amenable to isolation of patients with minimal construction
- Feasibility of controlling access to the facility and to each room
- Availability of potable water, bathroom, and shower facilities
- Facilities for patient evaluation, treatment, and monitoring
- Capacity for providing basic needs to patients
- Rooms and corridors that are amenable to disinfection
- Facilities for accommodating staff
- Facilities for collecting, disinfecting, and disposing of infectious waste
- Facilities for collecting and laundering infectious linens and clothing
- Ease of access for delivery of patients and supplies
- Legal/property considerations

Additional considerations include:

- Staffing and administrative support
- Training
- Ventilation and other engineering controls
- Ability to support appropriate infection control measures
- Availability of food services and supplies
- Ability to provide an environment that supports the social and psychological well-being of patients
- Security and access control
- Ability to support appropriate medical care, including emergency procedures
- Access to communication systems that allow for dependable communication within and outside the facility
- Ability to adequately monitor the health status of facility staff

QUARANTINE FACILITIES

Home quarantine

A person's residence is generally the preferred setting for quarantine. As with isolation, home quarantine is often least disruptive to a person's routine. Because persons who have been exposed to influenza may need to stay in quarantine for as long as 10 days (may be modified based on information about the virus), it is important to ensure that the home environment meets the individual's ongoing physical, mental, and medical needs. An evaluation of the home for its suitability for quarantine should be performed, ideally before the person is placed in quarantine. This evaluation may be performed on site by a health official or designee. However, from a practical standpoint, it may be more convenient to evaluate the residence through the administration of a questionnaire to the individual and/or the caregiver. Factors to be considered in the evaluation include:

- Basic utilities (water, electricity, garbage collection, and heating or air-conditioning as appropriate)
- Basic supplies (clothing, food, hand-hygiene supplies, laundry services)
- Mechanism for addressing special needs (e.g., filling prescriptions)

- Mechanism for communication, including telephone (for monitoring by health staff, reporting of symptoms, gaining access to support services, and communicating with family)
- Accessibility to healthcare workers or ambulance personnel
- Access to food and food preparation
- Access to supplies such as thermometers, fever logs, phone numbers for reporting symptoms or accessing services, and emergency numbers (these can be supplied by health authorities if necessary)
- Access to mental health and other psychological support services.

Quarantine in a community-based facility

Although the home is generally the preferred setting for quarantine, alternative sites for quarantine may be necessary in certain situations. For example, persons who do not have a home situation suitable for this purpose or those who require quarantine away from home (e.g., during travel) will need to be housed in an alternative location. Because persons who have been exposed to influenza may require quarantine for as long as 10 days, it is important to ensure that the environment is conducive to meeting the individual's ongoing physical, mental, and medical needs. Ideally, one or more community-based facilities that could be used for quarantine should be identified and evaluated as part of influenza preparedness planning. The evaluation should be performed on site by a public health official or designee. Additional considerations, beyond those listed above for home quarantine, include:

- Adequate rooms and bathrooms for each contact
- Delivery systems for food and other needs
- Staff to monitor contacts at least daily for fever and respiratory symptoms
- Transportation for medical evaluation for persons who develop symptoms
- Mechanisms for communication, including telephone (for monitoring by health staff, reporting symptoms, gaining access to support services, and communicating with family)
- Adequate security for those in the facility

Services for removal of waste. No special precautions for removal of waste are required as long as persons remain asymptomatic.

supplement 9
managing travel-related risk of disease transmission

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SUMMARY OF PUBLIC HEALTH ROLES AND RESPONSIBILITIES IN MANAGING TRAVEL-RELATED RISK OF DISEASE TRANSMISSION

INTERPANDEMIC AND PANDEMIC ALERT PERIODS

State and local responsibilities:

- Improve readiness to implement travel-related disease containment measures.
- Work with CDC quarantine stations and federal partners to provide public health information to travelers who visit countries where avian or animal influenza strains that can infect humans (e.g., avian influenza A [H5N1]) or human strains with pandemic potential have been reported.
- Work with CDC quarantine stations and federal partners to evaluate and manage arriving ill passengers who might be infected with avian or animal influenza strains (e.g., avian influenza A [H5N1]) or human strains with pandemic potential.

HHS responsibilities:

- Work with state and local health departments to prevent the importation of influenza-infected birds and animals into the United States.
- Provide state and local health departments with legal preparedness templates for use in implementing quarantine and patient isolation measures.
- Work with travel industry partners to ensure that airplane and cruise ship captains and crew are familiar with procedures for identifying and managing arriving ill passengers.
- Coordinate with other countries and WHO to prevent the spread of novel influenza via international travel.

PANDEMIC PERIOD

State and local responsibilities:

- Minimize travel-related disease transmission using a range of containment strategies.
- Evaluate the need to implement or terminate travel-related containment measures as the pandemic evolves.

HHS responsibilities:

- Work with state and local health departments and CDC quarantine stations to prevent the importation and exportation of cases of pandemic influenza.
- Promote a process of active engagement and discussion with state and local partners to support local decision-making on implementation of travel restrictions and other travel-related containment strategies.
- Coordinate with other countries and WHO to prevent the spread of pandemic influenza via international travel.

S9-I. RATIONALE

The 2003 pandemic of severe acute respiratory syndrome (SARS) demonstrated how quickly human respiratory viruses can spread, especially in a world of modern air travel (Appendix 1). Disease spread will likely be even faster during an influenza pandemic because a typical influenza virus has a shorter average incubation period (typically 2 days vs. 7-10 days for SARS-associated coronavirus [SARS-CoV]) and is more efficiently transmitted from person to person.

If an influenza pandemic begins outside the United States, public health authorities might screen inbound travelers from affected areas to decrease disease importation into the United States. If a pandemic begins in or spreads to the United States, health authorities might screen outbound passengers to decrease exportation of disease. Early in a pandemic, state and local health departments might also implement domestic travel-related measures to slow disease spread within the United States.

Because some persons infected with influenza will still be in the incubation period, be shedding virus asymptomatically, or have mild symptoms, it will not be possible to identify and isolate all arriving infected or ill passengers and quarantine their fellow passengers. Moreover, if an ill passenger is identified after leaving the airport, it might not be possible to identify all travel contacts within the incubation period for influenza. Nevertheless—depending on the situation—these activities might slow spread early in a pandemic, allowing additional time for implementation of other response measures such as vaccination.

Once a pandemic is underway, exit screening of travelers from affected areas ("source control") is likely to be more efficient than entry screening to identify ill travelers. Early in a pandemic, this intervention may decrease disease introductions into the U.S. Later, however, as pandemic disease spreads in communities, ongoing indigenous transmission will likely exceed new introductions and, therefore, federal authorities might modify or discontinue this strategy. Voluntary limitations on travel during a pandemic alert and pandemic, as persons decide to limit their own personal risk by canceling nonessential trips, will also decrease the amount of disease spread. Limiting or canceling travel of U.S. residents and others from affected countries will depend on the properties pf the pandemic virus that emerges, and will be informed by the facts on the ground at the time of emergence.

S9-II. OVERVIEW

Supplement 9 provides recommendations to state and local partners on travel-related containment strategies that can be used during different phases of an influenza pandemic. These strategies range from distribution of travel health alert notices, to isolation and quarantine of new arrivals, to restriction or cancellation of nonessential travel. State and local health departments will implement these strategies in coordination with CDC quarantine stations located at 18 U.S. ports of entry (Box 1). The recommendations for the Interpandemic and Pandemic Alert Periods focus on preparedness planning and on management of arriving ill passengers on international flights or cruise ships. The recommendations for the Pandemic Period focus on travel-related measures to decrease disease spread into, out of, and within the United States.

S9-III. RECOMMENDATIONS FOR THE INTERPANDEMIC AND PANDEMIC ALERT PERIODS

A. Preparedness for implementation of travel-related containment measures

If a pandemic begins outside the United States, early application of travel-related control measures (i.e., identification and isolation of ill travelers, quarantine of close contacts) might slow the introduction of the virus into the United States, allowing more time for healthcare preparedness efforts. The effectiveness of these measures might be limited because asymptomatic travelers can transmit disease, travelers in the incubation phase might not become symptomatic until after arrival at their

destinations, and it might not be possible to trace contacts within the incubation period for influenza. Results of mathematical models suggest that even with international flights, if persons are asymptomatic but incubating influenza when they board, they may remain asymptomatic when they arrive and therefore may not be detected by either exit or entry screening. Nevertheless, the ability to detect some cases early in the pandemic may slow disease spread even for a short time.

The effective implementation of travel-related containment measures depends on advance planning, preparedness, and coordination at the state, local, federal and international levels. This section provides information on engagement of partners, protocols for managing ill travelers, quarantine preparedness at ports of entry, and legal preparedness.

1. Engaging community partners

- In collaboration with the CDC, state and local planning for managing travel-related disease risk during a Pandemic Alert and Pandemic Period might include:
  - Quarantine officers
  - First responders (firefighters, police officers)
  - Local members of the legal community
  - Emergency medical services and other emergency responders
  - Hospital personnel
  - Representatives of airports, seaports, and the transportation industry, including unions
  - Political leaders
  - American Red Cross and other humanitarian organizations
  - Business services
- In collaboration with these partners, state and local health departments should:
  - Develop plans for training, mobilizing, and deploying public health staff and other emergency workers.
  - Conduct exercises and drills at ports of entry.
  - Train healthcare workers and emergency responders in the use of personal protective equipment (PPE) (see **Supplement 4**).
- State and local health departments should work with quarantine officers to develop memoranda of agreement with hospitals near ports of entry that are equipped to isolate, evaluate, and manage suspected influenza patients (see **Supplement 8**) and with emergency medical services that can help perform on-site assessments of ill passengers and transport them to hospitals for evaluation.

2. Protocols for managing ill travelers at ports of entry

- In collaboration with law enforcement authorities and other partners, public health officials and quarantine officers should develop protocols for managing ill arriving passengers identified by airplane or cruise ship personnel. The protocols should include provisions for:
  - Meeting flights with a reported ill passenger
  - Establishing notification procedures and communication links among organizations involved in the response

- Reporting potential cases to CDC (see **Supplement 1**)
- Providing a medical assessment of the ill traveler and referral for evaluation and care
- Separating the ill traveler from other passengers during the initial medical assessment
- Transporting the ill traveler to a designated healthcare facility (see also **Supplement 8**)
- Identifying other ill passengers and separating them from passengers who are not sick
- Transporting and quarantining contacts, if necessary (see 3 below)
- Enforcing isolation and quarantine, if necessary, when ill travelers or their contacts are uncooperative

- CDC is working with partners in the travel industry to ensure that airplane and cruise ship personnel are familiar with:
  - Case definitions (e.g., symptoms, travel history) for avian influenza A (H5N1) and other novel influenza strains of public health concern as they arise. CDC will provide additional and updated case definitions, as necessary, during the Pandemic Alert and Pandemic Periods.
  - Actions to take and persons to contact at their home offices, local quarantine station, or CDC if they are concerned about a sick passenger who might have novel influenza

3. Quarantine preparedness at ports of entry

- State and local public health officials, in collaboration with the CDC should identify quarantine facilities for housing passengers, crew, and emergency workers who may have been exposed to an ill traveler. These facilities should be equipped for:
  - Temporary quarantine (a few days), until the results of diagnostic tests become available
  - Longer-term quarantine (up to 10 days) if a diagnosis of pandemic influenza is confirmed
- State and local health departments and community partners should plan for the provision of goods and services to persons in quarantine (see Supplement 8).

4. Legal preparedness

While the federal government is primarily responsible for preventing the introduction, transmission, and spread of communicable diseases from foreign countries into the U.S., state and local health authorities may also take measures, such as quarantine of ill travelers and their contacts, to prevent the spread of communicable diseases within their borders. State and local authorities are primarily responsible for restricting travel within their borders while the federal government may take measures to prevent the interstate spread of communicable diseases.

Because jurisdictions and authorities at airports and other ports of entry overlap, local, state, and federal health authorities should establish protocols and outline roles and responsibilities in advance of a public health emergency. To be adequately prepared for management of travel-related risks, state and local health departments should:

- Ensure that legal authorities for the isolation of ill persons and the quarantine of exposed persons (at the local, state, and federal levels) are known and understood (see Supplement 8).
- Develop procedures for addressing overlapping multi-jurisdictional issues.

- Ensure legal authorities and develop protocols for:
  - Requirements for pre-departure screening of international and domestic travelers
  - Requirements for arrival screening and/or quarantine of international and domestic travelers
  - Prohibitions on travel by ill persons and their contacts
  - Restrictions on use of mass transit systems
  - Cancellation of nonessential travel
- Work closely with local, state, and federal law enforcement officials to develop plans and protocols for enforcing travel restrictions, if necessary.

B. Health information for travelers

CDC's Travelers' Health website (www.cdc.gov/travel/) will provide up-to-date travel notices for international travelers to countries affected by novel influenza viruses during the Pandemic Alert Period and Pandemic Period. These notices are issued depending on the scope, risk for travelers, and recommended preventive measures. Four types of travel notices can be issued: In the News, Outbreak Notices, Travel Health Precautions, and Travel Health Warnings. Additional Travel Health Precautions or Warnings (see Box 2) may be issued to inbound and outbound travelers during the Pandemic Alert Period if avian influenza spreads internationally and causes additional cases of human influenza.

C. Evaluation of travel-related cases of infection with novel strains of influenza

During the Pandemic Alert Period, travel-related cases of infection might be detected after entry into the United States or reported during transit by airline or cruise ship personnel before arrival of an ill passenger. Information on the detection and identification of novel strains of influenza is provided in **Supplement 1**. Guidance on the clinical management of suspected cases of novel influenza is provided in **Supplement 5**.

1. Managing ill passengers

- State and local health departments should follow protocols prepared in advance for the management of arriving ill passengers who meet the clinical and epidemiologic criteria for infection with a novel strain of influenza. Additional or updated case definitions for infection with novel strains of influenza will be issued, as needed, if the level of heightened surveillance increases from a situation of little immediate pandemic risk (corresponding to WHO Pandemic Alert Phase 3), to one in which pandemic risk is moderate or substantial (corresponding to WHO Pandemic Alert Phases 4 or 5).
- If an ill passenger with a suspected case of novel influenza is reported aboard an arriving airplane or cruise ship, a state or local health official or quarantine officer should do the following:
  - All partners should be notified, including the nearest Quaratine station, state and local authorities, and the CDC.
  - Request information on the ill passenger's symptoms and travel and exposure history to make an initial assessment if the illness meets the current clinical and epidemiologic criteria for avian influenza A (H5N1) or is suspicious for a novel influenza strain.
  - Determine if a state or local public health worker and/or quarantine officer should meet the airplane or cruise ship to further evaluate the ill traveler.
  - Provide the crew with guidance on infection control procedures, if needed (e.g., separate the ill passenger as much as possible from other passengers; provide the ill passenger with a mask or tissues to cover coughs and sneezes).
- If a state or local public health worker and/or quarantine officer decides to meet the airplane or cruise ship and perform an initial medical evaluation of the ill traveler, the passengers and crew should be informed of the situation and should not be allowed to disembark until the evaluation is complete.

- If public health officials determine that the ill passenger meets the clinical and epidemiologic criteria for infection with a novel influenza strain, the patient should be sent by ambulance to a hospital, using appropriate infection control procedures for transit and patient isolation (see **Supplement 4**).[1]

2. Managing travel contacts

- Local and/or state health departments, in consultation with CDC, should decide how to manage an ill person's travel contacts on a case-by-case basis, taking into consideration the following factors:
- Likelihood that the suspected case is due to a novel influenza strain (based on symptoms and travel history, if laboratory results are not available)
- Likelihood that the causative virus is transmitted from person to person with a moderate or high efficiency (as in later phases of the Pandemic Alert Period)
- Feasibility of tracing and monitoring travel contacts, as well as the patient's family members, workmates, schoolmates, and healthcare providers

- Management of contacts might include:
  - Passive or active monitoring without activity restrictions
  - Quarantine at home or in a designated facility, and/or
  - Antiviral prophylaxis or treatment.

For retrospectively identified cases, if passengers and crew members cannot be traced within 48-72 hours of the presumed exposure, local and/or state health departments, in consultation with CDC, might consider other options (e.g., issue a public notice through the news media).

- During the Pandemic Alert Period, especially during the earlier phases, health departments should quarantine travel contacts (i.e., passengers, crew, response workers) **only when there is a high probability that the ill passenger is infected with a novel influenza strain that is transmitted between people.**

  If a decision is made to initiate quarantine, persons who cannot be quarantined at home should be housed in a pre-designated temporary care facility until the diagnosis of the ill passenger is confirmed or disproved. Each quarantined person should receive a preliminary medical assessment and should be interviewed to ascertain their travel and exposure histories.
- If the diagnosis of a novel strain of influenza is confirmed, quarantined persons should be transferred as soon as possible to a pre-designated longer-term quarantine facility and should remain there for the maximum length of the incubation period for influenza. Each quarantined person may receive antiviral medication and should be monitored twice a day for fever and other signs of influenza (see **Supplement 8**).
- Medical follow-up and travel assistance should be provided to all quarantined persons when the quarantine period is over.

D. Preventing the importation of infected birds and animals

State health departments should continue to assist federal agencies with responsibility for preventing the shipment of infected birds and animals into the United States. Federal agencies with responsibility for inspecting imported animals, implementing veterinary quarantine orders, and enforcing U.S. Department of Agriculture (USDA) trade bans and HHS import bans include

[1] Protocols and memoranda of agreement with ambulance service adn hospitals with appropriate infection control measures in place should be established.

the Animal and Plant Health Inspection Service (APHIS), USDA; HHS/CDC; Bureau of Customs and Border Protection, Department of Homeland Security; and U.S. Fish and Wildlife Service, Department of the Interior.

USDA regulates the importation of all avian species (poultry, pet birds, birds exhibited at zoos, ratites) into the United States (9 CFR, Part 93). In general, birds submitted for entry into the United States must be quarantined in USDA-approved facilities. During quarantine, avian influenza virus isolation is attempted on samples collected from all dead birds and some live birds. These precautions are taken to prevent the introduction of exotic avian diseases, including avian influenza, into the United States. USDA import procedures for avian species are provided at www.aphis.usda.gov/vs/ncie/importing.html.

Under section 316 of the PHS Act (42 USC 264) the HHS Secretary may make and enforce regulations necessary to prevent the introduction, transmission, and spread of communicable disease from foreign countries into the U.S. and from one state or possession into any other state or possession. CDC has implemented this statute through regulations and those that authorize CDC's order banning birds and bird products that might carry avian influenza A (H5N1) can be found at 42 CFR 71.32(b). A current listing of CDC's orders banning the importation of birds and bird products that might carry avian influenza A (H5N1) can be found at www.cdc.gov/flu/avian/outbreaks/embargo.htm.

S9-IV. RECOMMENDATIONS FOR THE PANDEMIC PERIOD

Over the course of an influenza pandemic, state and local health authorities might consider a range of travel-related control measures to decrease the spread of disease into the United States, out of the United States (Appendix 2), or within the United States. The following factors may be considered in developing policy:

- The relative magnitude, duration, and stage of indigenous transmission versus the risk associated with further introduced cases. When pandemic disease is widespread in the U.S., the additional contribution of introduced cases to the magnitude or spread of the pandemic will be minimal depending on the state of the epidemic in the specific location of introduction.
- The value of compulsory restrictions in a setting of voluntary changes in travel patterns. Voluntary changes in travel will occur during a pandemic as persons choose to cancel nonessential travel to decrease their potential exposure and risk of acquiring influenza infection. In this context, the added value of compulsory restrictions should be considered relative to the societal disruptions that limitations on movement would cause.

HHS will promote an active process of engagement and discussion to help states and localities decide on which actions to take as the situation evolves. Because travel-related measures implemented by one jurisdiction will inevitably affect others, communication, collaboration, and especially coordination before any measures are implemented is crucial.

A. Travel-related containment measures

1. Travel into the United States

Early during an influenza pandemic that begins outside the United States, health authorities will heighten disease surveillance at U.S. airports and seaports and maintain close communication with WHO, foreign governments, and the airline industry. Travel-related disease control measures will include management of ill travelers arriving at ports of entry and provision of travel health alert notices to incoming travelers.

a) Managing arriving ill passengers

Identification and management of incoming ill travelers may delay and decrease the introduction of novel influenza strains into the United States during the Pandemic Alert Period. These efforts will continue during the early stages of the Pandemic Period, especially if a pandemic strain emerges in another country but has not yet entered the United States.

Once the pandemic has spread outside and within the United States, screening for arriving ill passengers will become less useful and feasible. Although exit-screening of travelers from affected areas ("source control") is likely to be a more effective disease control measure, its effectiveness too will be limited.

To manage arriving ill passengers, public health authorities or quarantine officers should do the following:

- If a suspected case of pandemic influenza is reported aboard an arriving airplane or cruise ship during the early stages of a pandemic, obtain preliminary information about the ill passenger, and advise the captain and crew on patient isolation and infection control.
- If the likelihood of pandemic influenza infection appears high, consider these actions:
  - Notify the airport to mobilize its first responders, and arrange for patient transport and preparation of quarantine facilities.
  - Meet the airplane or cruise ship, perform a medical evaluation of the ill traveler, and assess the risk to public health.
  - Inform the passengers and crew of the situation, and do not allow them to disembark until the evaluation is complete. Procedures for medical management of the patient, passengers, and crew are described in S9-III.C.

b) Travel health precautions and warnings

As the pandemic spreads from country to country, HHS will update country-specific travel notices and post them on the CDC Travelers' Health website (http://www.cdc.gov/travel/). Advisories might include:

- **Travel Health Precautions** that describe steps that can be taken to reduce the risk of infection (e.g., avoiding travel to high-risk settings and communities where transmission is occurring)
- **Travel Health Warnings** that recommend postponement of nonessential travel

c) Travel-related measures at early stages of a pandemic

When there is limited transmission in other countries and potential for importation of cases into the United States, HHS and state and local health departments might consider the following actions:

- Initiate enhanced disease surveillance at ports of entry.
- Provide guidance on infection control procedures that can be implemented, if needed, on airplanes or ships (e.g., separate the ill passenger from other passengers; provide the ill passenger with a mask or tissues to prevent viral spread via coughing).
- Isolate arriving ill passengers, and quarantine their contacts as necessary.
- Collect information on all arriving passengers if notification is warranted (e.g., for antiviral administration, vaccination, or health monitoring).

d) Travel-related measures at later stages of a pandemic

If the situation worsens overseas and there is extensive and sustained transmission in other countries, HHS and state and local health departments might consider these actions:

- Distribute travel health alert notices to passengers arriving from affected countries (i.e., countries for which health warnings have been issued).
- Post travel health alert notices in airports (e.g., on posters).

- Arrange with airline industry partners to show videos or public announcements about pandemic influenza on airplanes or cruise ships arriving from affected countries.
- Recommend canceling or limiting nonessential travel to affected countries.
- Collect information on all arriving passengers if notification is warranted (e.g., for antiviral administration, vaccination, or health monitoring).

Decisions regarding the implementation of these actions may depend on how widely the pandemic disease has spread within the U.S.

Other potential control measures might include increasing disease surveillance among passengers arriving from affected countries by visually inspecting travelers as they disembark, screening travelers for fever or other influenza symptoms, or administering questionnaires on possible exposures to influenza (e.g., contacts with influenza patients or visits to high-risk areas). Experience during the 2003 SARS outbreak (Appendix 1) suggests that implementation of these measures—which are highly labor-intensive and of unproven benefit—would be especially burdensome during an influenza pandemic. However, it is possible that the transmissibility of a unique pandemic strain may differ from that of seasonal influenza strains or SARS, warranting consideration of alternative measures.

2. Travel out of the United States

If the level of influenza transmission in the United States presents a high risk for exportation of disease, HHS and state and local health authorities should consider the following actions:

- Distribute travel health warnings to outbound passengers who live in or have visited affected parts of the United States.
- Recommend the cancellation of nonessential travel to other countries from ports of entry in affected parts of the United States.
- Implement pre-departure screening (e.g., temperature screening or visual screening) of outbound travelers.

3. Travel within the United States

- If the level of influenza transmission in a U.S. area is high and if most other areas have not yet been affected, HHS and state and local health authorities might decide to recommend limiting or canceling nonessential travel to that area or to implement increased disease surveillance measures.
- Other containment measures and travel restrictions to slow disease spread within the United States that might be considered include:
  - Distributing travel health alert notices on domestic flights
  - Isolating ill arriving passengers on domestic flights and quarantining passengers and crew, following protocols developed for international flights (see S9-III.C)
  - Closing mass transit systems (e.g., buses and subways; see **Supplement 8**)
  - Closing interstate bus and train routes

The potential effectiveness of these measures (see S9-IV) and the feasibility of implementing them should be considered in decision-making.

B. De-escalation of travel-related control measures

Decisions to de-escalate control measures related to international travel will be made in consultation with WHO.

1. Outbound passengers

CDC will downgrade a Travel Health Warning for outbound U.S. passengers to a Travel Health Precaution for a given country or area when there is adequate and regularly updated reporting of surveillance data from the area, and limited or no recent instances of cases in the area.

2. Inbound passengers

On arrival, inbound passengers from areas under a Travel Health Warning should be provided with travel health alert notices. Because it is often difficult to determine passengers' points of origin, it may be more practical to continue providing travel health alert notices until Travel Health Precautions have been lifted for all areas.

CDC will remove a Travel Health Precaution when there is adequate and regularly updated reporting of surveillance data from the area and limited or no recent instances of cases exported from the area.

BOX 1. CDC QUARANTINE STATIONS

CDC operates 18 quarantine stations that are responsible for preventing the introduction of infectious diseases of public health importance into the United States. The stations are located at major international airports in Los Angeles, San Francisco, Seattle, Miami, Honolulu, Chicago (O'Hare), New York City (JFK), Atlanta, Houston, El Paso, and Washington, DC. Each station also covers other ports of entry (airports, seaports, land borders) in the region. The stations' quarantine officers evaluate ill passengers who are identified by flight crews, U.S. Customs Service inspectors, or other Federal Inspection Service[1] personnel. Quarantine inspectors also work with regulatory agencies to inspect imported animals and other cargo (http://www.cdc.gov/ncidod/dq/quarantine_stations.htm).

Some ports of entry (with and without quarantine stations) have local physicians on call, and HHS has an ongoing program to establish agreements with local hospitals that accept patients referred by quarantine station staff.

[1] Federal Inspection Service agencies include the Animal and Plant Health Inspection Service (APHIS/USDA), Centers for Disease Control and Prevention (CDC/HHS), Customs and Border Protection (CBP/DHS), and Food Safety and Inspection Service (FSIS/USDA).

BOX 2. TRAVEL-RELATED DEFINITIONS

Travel Notices: Different types of notices for international travelers. During the 2003 SARS outbreak, CDC issued two types of travel notifications about disease occurrences in specific geographic areas. A travel alert, a lower-level notice, provided information on the outbreak and informed travelers about how to reduce their risk of acquiring infection. When the health risk for travelers was thought to be high, CDC issued a travel advisory recommending against nonessential travel to the area. Travel advisories were intended to reduce the number of travelers to high-risk areas and the risk for spreading disease to other areas. The levels of notification have since been revised to include four types of travel notices: In the News, Outbreak Notice, Travel Health Precautions, and Travel Warnings.

In the News: Notification by CDC of an occurrence of a disease of public health significance affecting a traveler or travel destination. The purpose is to provide information to travelers, Americans living abroad, and healthcare providers. "In the News" is issued when the risk for disease exposure is not increased beyond the usual baseline risk for that area, and only standard guidelines are recommended.

Outbreak Notice: Notification by CDC that an outbreak of a disease is occurring in a limited geographic area or setting. The purpose is to provide information to travelers, Americans living abroad, and healthcare providers about the status of the outbreak and to remind travelers about standard or enhanced travel recommendations for the area. Outbreak Notices are issued when the risk for disease exposure is increased but well defined and limited to specific settings.

Travel Health Precaution: Notification by CDC that a disease outbreak of significant scope is occurring in a large geographic area. The purpose is to provide information to travelers, Americans living abroad, and healthcare providers about the status of the outbreak (its magnitude, scope, and rapidity of spread), specific precautions to reduce the risk of infection, and what actions to take if they become ill. Travel Health Precautions are issued when the risk for the individual traveler is increased in defined settings or associated with specific risk factors (e.g., transmission in a healthcare or hospital setting). Travel Health Precautions do NOT recommend canceling travel to the area.

Travel Health Warning: Notification by CDC that a widespread outbreak of a disease of public health concern is expanding outside the area or populations that were initially affected. The purpose is to provide information to travelers, Americans living abroad, and healthcare providers about the status of the outbreak (its magnitude, scope, and rapidity of spread), specific precautions to reduce the risk of infection, and what actions to take if they become ill. **Travel Health Warnings recommend canceling nonessential travel to the area** because the risk for the traveler is considered high (i.e., there is evidence of transmission outside defined settings and/or inadequate containment). Additional preventive measures may be recommended, depending on the circumstances (e.g., travelers may be requested to monitor their health for a certain period after their return; arriving passengers may be screened at ports of entry). A Travel Health Warning may reduce the volume of traffic to an affected area, which in turn can reduce the risk of disease spread to previously unaffected sites.

Travel Health Alert Notice: Notice with travel-related information and recommendations designed for inbound travelers.

Travel contact: A person on the same conveyance as the ill person.

Close contact: A person who has cared for or lived with the ill person or had a high likelihood of direct contact with respiratory secretions and/or body fluids of the ill person. Examples of close contact with an ill person include kissing or hugging, sharing eating or drinking utensils, talking within 3 feet, and direct touching. Close contact does not include activities such as walking by a person or briefly sitting across a waiting room or office.

APPENDIX 1. RECENT EXPERIENCE WITH TRAVEL-RELATED CONTAINMENT MEASURES: THE 2003 SARS OUTBREAK

During the 2003 global response to severe acute respiratory syndrome (SARS), the control strategy for the United States included issuing travel notifications, distributing Travel Health Alert Notices to travelers arriving from areas with SARS, and conducting visual inspections of arriving travelers to facilitate early identification of imported cases and response to reports of ill passengers. CDC staff met more than 11,000 direct and indirect flights from SARS-affected areas and distributed more than 2.7 million Travel Health Alert Notices to arriving passengers as well as to persons arriving at 13 U.S. land border crossings near Toronto and departing passengers bound for the United States from the Toronto airport. Travel Health Alert Notices informed returning travelers of potential exposure to SARS-associated coronavirus (SARS-CoV). They alerted travelers to the symptoms of SARS-CoV disease and advised them to promptly seek medical attention if symptoms developed. The notices also provided information and instructions for physicians.

During the SARS outbreak response, CDC quarantine staff met planes reporting an ill passenger to facilitate 1) evaluation of the passenger for possible SARS-CoV disease, 2) collection of locating information on the other passengers, and 3) coordination with federal and local authorities. If the ill passenger was determined to be a possible SARS case, the locating information was forwarded to state and local health departments for contact tracing.

Border and travel-related activities implemented in countries more seriously affected by SARS included pre-departure temperature and symptom screening, arrival screening (asking passengers about travel history and possible exposure to SARS-CoV), "stop lists" (maintaining lists of persons who were possible SARS cases or contacts to prevent them from traveling), and quarantine of travelers returning from other SARS-affected areas.

Lessons learned from this response include the following:

- SARS-CoV can spread rapidly on a global scale through international travel if control measures are not implemented.
- SARS-CoV transmission can be halted through aggressive global measures to educate, detect cases early, effectively isolate cases, and identify, monitor, and quarantine contacts.
- Patients with SARS can transmit infection to other passengers on conveyances and should postpone travel until they are no longer infectious.
- SARS-CoV transmission can occur within the close confines of conveyances. Resulting infections usually represent a failure to recognize symptomatic index cases and their high-risk contacts who should have been prevented from traveling.
- Active follow-up of passengers on conveyances with SARS cases can help prevent further spread by informing passengers of their exposure and providing instructions for monitoring their health and seeking medical evaluation if they become ill.

While these lessons may have some relevance, their applicability to an influenza pandemic is limited by the substantial differences between the epidemiology of transmission of influenza and SARS-CoV. The much shorter incubation period and intergenerational period for influenza compared with SARS-CoV poses enormous time challenges to case isolation, contact tracing, and selective individual quarantine. The possibility of influenza virus transmission by asymptomatic persons makes the ability to effectively implement control measures such as selective quarantine necessarily incomplete and potentially decreases the impact significantly. In addition, with SARS-CoV, peak communicability occurred most often during the second week of illness when cases were extremely ill and often hospitalized; this enabled containment to focus heavily on institutional infection control measures. Influenza virus transmission will occur much earlier in relation to illness onset and is expected to

be preferentially community-acquired rather than nosocomial. Finally, there were fewer than 10,000 documented human cases of SARS worldwide whereas past influenza pandemics have caused symptomatic infection in about 30% of the U.S. population. Thus, in the current U.S. population alone there would be almost 90 million illnesses, and many more persons would have asymptomatic infections. Given the vastly greater number of persons who will be spreading influenza infection within and between communities, approaches to control will inevitably need to be different.

APPENDIX 2. TRAVEL-RELATED INFLUENZA RESPONSE MATRICES

Matrix 1: Inbound Travel

Level of influenza transmission	Suggested actions to manage inbound travel
Potential for imported cases in the United States and limited transmission (clusters of human-to-human cases or second-generation spread) in the inbound traveler's location of origin	CDC will distribute travel health alert notices to all arrivals. **Suggested actions:** • Consider enhanced disease surveillance at ports of entry. • Request information on the ill passenger's symptoms and travel and exposure histories. • Determine if a state or local public health worker and/or CDC quarantine officer should meet the airplane or cruise ship to further evaluate the ill traveler. • Provide the crew with guidance on infection control procedures, if needed (e.g., separate the ill passenger as much as possible from other passengers; provide the ill passenger with a mask or tissues to prevent viral spread via coughing). • Isolate arriving ill passengers, and quarantine their contacts, as necessary.
Imported cases in the United States and extensive transmission in the inbound traveler's location of origin	**Additional actions:** • Consider prohibiting all nonessential arrivals. • Consider active monitoring of all arriving passengers for fever and respiratory symptoms.
Extensive transmission in the inbound traveler's location of origin	**Additional actions:** • Prohibit all nonessential arrivals.

APPENDIX 2. TRAVEL-RELATED INFLUENZA RESPONSE MATRICES (CONT.)

Matrix 2: Outbound Travel

Level of influenza transmission	Suggested actions to manage outbound travel
Limited transmission (clusters of human-to-human cases or second-generation spread) in the outbound traveler's destination	CDC will issue Travel Health Precautions and Travel Health Warnings for particular destinations, as needed. **Suggested actions:** • Distribute targeted health education messages to outbound travelers.
Extensive transmission in the outbound traveler's destination	**Additional actions:** • Arrange with airline industry partners to show videos or air public announcements about pandemic influenza on airplanes and cruise ships. • Cancel or limit nonessential travel to affected countries.
Extensive transmission in the outbound traveler's destination and in the United States.	**Additional actions:** • Consider implementing medical screening at exit points in the United States.

supplement 10
public health communications

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SUMMARY SUMMARY OF PUBLIC HEALTH ROLES AND RESPONSIBILITIES IN PUBLIC HEALTH COMMUNICATIONS

INTERPANDEMIC AND PANDEMIC PERIODS

State and local responsibilities:

- Assess and monitor readiness to meet communications needs in preparation for an influenza pandemic, including regular review and update of communications plans.
- Plan and coordinate emergency communication activities with private industry, education, and nonprofit partners (e.g., local American Red Cross chapters).
- Identify and train lead subject-specific spokespersons.
- Provide public health communications staff with training on risk communications for use during an influenza pandemic.
- Develop and maintain up-to-date communications contacts.
- Participate in tabletop exercises and other collaborative preparations to assess readiness.
- Address rumors and false reports regarding pandemic influenza threats.
- Confirm any contingency contracts needed for communications resources during a pandemic

HHS responsibilities:

- Develop a Communications and Public Engagement Strategy for Pandemic Influenza (see appendix 4)
- Develop key messages and materials, conduct audience research and message testing, and share results with international, other Federal departments, state and local communications staff. Materials will be available on www.pandemicflu.gov.
- Coordinate pandemic influenza media messages to ensure consistency.
- Provide tools and resources through the www.pandemicflu.gov and www.cdc.gov/flu/ websites and other avenues to help educate state and local communications staff.
- Identify and train lead spokespersons.
- Provide state and local health agencies with guidance about developing and integrating communications aspects of preparedness plans.
- Work with state and local governments to incorporate communications preparedness as part of larger preparedness exercises.
- Provide regular updates about situations that pose potential pandemic influenza threats (e.g., through Health Alert Network [HAN] notices, Epi-X, and web postings).
- Distribute educational messages and materials about pandemic influenza and ways that people can protect themselves and their families.
- Distribute practical information, such as travel advisories, infection control measures, availability and appropriate use of antiviral medications and vaccines, and specific public health actions that may be advised.
- Address rumors and false reports regarding pandemic influenza threats and related issues.
- Coordinate international information exchange and communication strategies with WHO and other international partners, as appropriate.

SUMMARY OF PUBLIC HEALTH ROLES AND RESPONSIBILITIES (CONT.) IN PUBLIC HEALTH COMMUNICATIONS

PANDEMIC PERIOD

State and local responsibilities:

- Contact key community partners and implement frequent update briefings.
- As appropriate, implement and maintain community resources, such as hotlines and websites to respond to local questions from the public and professional groups.
- Tailor communications services and key messages to specific local audiences.
- In coordination with epidemiologic and medical personnel, obtain and track information daily on the numbers and location of newly hospitalized cases, newly quarantined persons, and hospitals with pandemic influenza cases. Use these reports to determine priorities among community outreach and education efforts, and to prepare for updates to media organizations in coordination with federal partners.

HHS responsibilities:

- Coordinate pandemic influenza media messages to ensure consistency across Federal government
- Coordinate communications activities with state and local communications staff, including regional or local communications centers as appropriate.
- Promptly respond to rumors and inaccurate information to minimize concern, social disruption, and stigmatization.
- Coordinate international information exchange and communication strategies

S10-I. RATIONALE

Strategic communications activities based on scientifically derived risk communications principles are an integral part of a comprehensive public health response before, during, and after an influenza pandemic. Effective communication guides the public, the news media, healthcare providers, and other groups in responding appropriately to outbreak situations and complying with public health measures.

The goals of **Supplement 10** are to:

- Describe the integral role of communications in preparing for, implementing, and evaluating public health actions to protect health and prevent pandemic influenza-associated morbidity and mortality.
- Provide local and state health officials, community healthcare professionals and communications specialistswith guidance to assist them in developing and implementing communication plans that support an effective public health response and help minimize anxiety, fear, and stigmatization.
- Provide the basis for a well-coordinated and consistent communications strategy across jurisdictions, based on a common adherence to established risk communication principles.

This supplement emphasizes the following strategies to help state and local communications professionals collaborate with each other, CDC, and other organizations to accomplish these goals:

- Provide timely, accurate, consistent, and appropriate information about pandemic influenza public health interventions.
- Emphasize the rationale and importance of adherence to public health measures that some people may consider intrusive (e.g., quarantine).
- Help set realistic expectations of public health and health care systems.
- Promptly address rumors, inaccuracies, and misperceptions.
- Minimize stigmatization that may occur during a pandemic.
- Adapt materials for others with special needs (e.g., non-English speaking populations, difficult-to-reach communities, and persons living in institutional settings) receive appropriate information.
- Acknowledge the anxiety, distress, and grief that people experience during long-term, major public health events such as pandemics.

S10-II. OVERVIEW

Communications preparedness for an influenza pandemic, as outlined in this supplement, follows seven key risk communications concepts.

- When health risks are uncertain, as likely will be the case during an influenza pandemic, people need information about what is known and unknown, as well as interim guidance to formulate decisions to help protect their health and the health of others.
- Coordination of message development and release of information among federal, state, and local health officials is critical to help avoid confusion that can undermine public trust, raise fear and anxiety, and impede response measures.
- Guidance to community members about how to protect themselves and their family members and colleagues is an essential component of crisis management.
- Information provided to the public should be technically correct and succient without seeming patronizing.
- Information presented during an influenza pandemic should minimize speculation and avoid over-interpretation of data, overly confident assessments of investigations and control measures.
- An influenza pandemic will generate immediate, intense, and sustained demand for information from the public, healthcare providers, policy makers, and news media. Healthcare workers and public health staff are likely to be involved in media relations and public health communications.
- Timely and transparent dissemination of accurate, science-based information about pandemic influenza and the progress of the response can build public trust and confidence.

During the Interpandemic Period, national, state, and local health communications professionals should focus on preparedness planning and on building flexible, sustainable communications networks. During the Pandemic Period, they should focus on well coordinated health communications to support public health interventions designed to help limit influenza-associated morbidity and mortality.

S10-III. RECOMMENDATIONS FOR THE INTERPANDEMIC AND PANDEMIC ALERT PERIODS

During the Interpandemic and Pandemic Alert Periods, health communications professionals should work together to develop and maintain communications preparedness and to keep the public and other target groups updated about risks as the threat of a pandemic evolves. Actions fall into four major categories:

- Assessing communications capacity and needs
- Conducting collaborative planning
- Developing and testing standard procedures for disseminating information
- Developing, testing, and disseminating locally tailored messages and materials

A. Assessing communications capacity and needs

A first step in effective risk communications preparedness is to conduct an assessment of communications strengths and challenges. Planning should include the following.

1. Capacity

- As part of overall pandemic influenza preparedness planning, develop a phased risk communications plan.
- Determine whether adequate human and fiscal resources will be available for all phases of a pandemic. If not, plan to augment these resources.
- Review or establish procedures to help ensure that technology such as networks, servers, and system backups are available, periodically tested, and integrated into overall planning for pandemic influenza. Identify and include other types of technology, such as faxes and mass mailing systems. Establish priorities and implement improvement plans for any technology deficiencies.
- Prepare for resource contingencies (e.g., surge capacity) by developing and regularly updating backup plans and procedures, identifying community resources, and training extra staff for emergency communications responsibilities.
- Ensure ongoing proficiency among all staff engaged in pandemic influenza response, especially given personnel changes, reorganization, or other variables.

2. Needs

- Review and update risk communications plans at least annually to ensure that they remain practical and evidence-based. Share the plans in advance with stakeholders.
- Identify communications professionals and media spokespersons; as needed, provide media training and instruction in crisis and risk communication. Encourage familiarity with professional counterparts from local/regional jurisdictions or communities to facilitate collaboration.
- Familiarize key officials with available communications resources and gaps; apprise policy and key decision-makers of plans to deploy staff and resources during an influenza pandemic.
- Prepare basic communications resources in advance, and plan to update them during a pandemic. Appendices 2 and 3 provide sample templates, fact sheets, and other communications tools that will be available through the www.pandemicflu.gov and www.cdc.gov websites, as well as links to other resources.
- Identify common communications opportunities or challenges with neighboring jurisdictions, particularly with regard to reaching people in high-priority risk groups; consider novel opportunities to pool communications resources.
- Continuously monitor the effectiveness of risk communication activities, adjusting as necessary to achieve public health communications objectives.

B. Conducting collaborative planning

Collaborative planning should begin as early as possible. Communications professionals in the public and private sectors need to ensure strong and well-integrated working relationships that will help sustain communications resources as a pandemic evolves. Federal interaction with WHO and other international partners is vital to surveillance and other essential information

exchange and to building collaborative and consistent messaging strategy. The following recommendations are critical elements of a comprehensive domestic response:

- When appropriate, coordinate training and other preparedness activities that include options for backing up key communications personnel in the event of their personal illness or emergency.
- Coordinate with partner agencies to prepare for appropriate public, healthcare provider, policy, and media responses to outbreaks of pandemic influenza. Be prepared to address the following topics as a pandemic alert draws near:
  - Basic health protection information the public and other target audiences will need
  - Responsiveness, capabilities, and limitations of the public health system
  - Roles and responsibilities of diverse pandemic response stakeholders
  - Resources to help people cope with escalating fear, anxiety, grief, and other emotions (see **Supplement 11**).
  - How public health procedures and actions may change during different pandemic phases and why unusual steps may be needed to protect public health.
- Consider when and how to use federal assistance when available. For instance, background information and frequent updates for communications and other healthcare professionals will be available on the www.pandemicflu.gov website and through other official mechanisms.
- Identify and engage credible local resources as partners. For example, local chapters of nonprofit health organizations may assist with urgent communications to community groups.
- Affirm mechanisms with news media representatives to optimize effective working relationships during pandemic phases.
- Ensure that communications professionals have opportunities to participate with other public health and emergency staff in tabletop exercises and drills to help identify and resolve potential problems in the Interpandemic and Pandemic Alert periods.

C. Developing and testing standard state and local procedures for disseminating information

Although there will be much that is unpredictable about an influenza pandemic, communication processes can and should be formalized. Standard, yet flexible procedures for disseminating information support consistency, efficiency, and coordination, and improve prospects for effective feedback in both internal and external communications.

State and local communication plans should identify dissemination procedures and channels for forwarding communications from federal agencies to ensure that partners and stakeholders at all levels remain informed but protected from redundant or unnecessary messaging. As an influenza pandemic unfolds, HHS and its agencies will relate essential information through well established channels and formats (e.g., CDC's Emergency Communication System).

The following recommendations can aid development of effective state and local information dissemination plans for use during an influenza pandemic:

- Establish expedited procedures for reviewing and approving pandemic influenza-related messages and materials.
- Establish protocols for frequently updated information, including daily disease activity reports. These may include morbidity and mortality figures, geographic location of cases, demographics of infected populations, and the number of persons hospitalized.
- Establish and maintain a website with current information.
- Work with local information technology (IT) professionals to identify development servers on which to build state or local emergency websites that can help manage information requests when needed. Consider whether to develop some

communications materials in advance and store them on these secure servers. Add the www.pandemicflu.gov website as a link to local websites. Also see other available links in Appendix 3.

- Federal hotlines, such as the CDC-INFO telephone line (1-800-CDC-INFO; 1-800-232-4636), will be available for public information. However, during an influenza pandemic, state and local health departments may also wish to tailor additional information for their localities. Determine if agreements or contracts will be needed to establish a local toll-free public information hotline. Hotline staff should be trained in advance. They should have access to the www.pandemicflu.gov website and to an evolving state or local database of frequently asked questions. Consider options for adapting existing networks into pandemic influenza response systems, either singularly or in combination with neighboring jurisdictions.
- Prepare contingency plans to manage increased media demands. Jurisdictions with possible or early confirmed cases of pandemic influenza can expect focused media attention. Local media relations specialists will need to prepare for media requests and facilities needs, especially for television. Regularly scheduled press briefings may reduce the volume of inquiries to press offices. Media interest may merit daily briefings.
- Develop ongoing coordination procedures with other agencies and organizations to conserve resources and avoid duplication in such areas as developing and pre-testing messages, and in training media spokespersons.

D. Developing, testing, and disseminating locally tailored Interpandemic messages and materials

The Interpandemic period is the ideal time to identify and learn about target audiences and raise awareness and knowledge of pandemic influenza. Doing so, however, may prove challenging. For instance, in the absence of pandemic influenza, it may be difficult to generate media and public interest in pandemic influenza. In addition, the need to inform and educate the public, healthcare professionals, policy-makers, and others about the threat of a pandemic must be balanced against the possibility that a pandemic may not occur for many years and may or may not be severe. Risk communication strategies such as dilemma-sharing and acknowledging uncertainty can help establish appropriate and balanced messages.

It is also appropriate during the Interpandemic Period to prepare communications materials for use during the Pandemic Alert and Pandemic Periods. Advance message development helps to ensure that the target audience's questions and concerns are addressed and that messages are credible and understandable. Answers to the most likely questions can be provided by way of press releases and fact sheets, using "place-holders" for specific details to be inserted later. Reviewing and clearing these materials in advance can help identify potential areas of disagreement and allow time to work through controversies outside the stressful environment of an emergency response. Formative research can help inform development of appropriately tailored messages. (See Appendices 1 and 2 for additional information about message development.)

Communications efforts should also take into account knowledge, attitudes, and beliefs (KABs) that suggest how audiences understand and react to certain messages. Concerns will vary by group or subgroup but will likely include personal safety, family and pet safety, and interruption of routine life activities. State and local communications professionals should identify methods to assess the unique KABs of target audiences in their populations and communities. Such activities can help identify potential barriers to compliance with response measures, and inform message development to build support and trust.

Stigmatization and discrimination (e.g., being shunned as a perceived source of contagion) can be especially difficult and potentially dangerous during an infectious disease outbreak. Identify possible scenarios when stigmatization may occur. Plan steps to address and resolve such problems quickly and repeatedly if needed. Consider messages for general audiences, high-risk groups, and difficult-to-reach populations. (For additional information, see Supplement 11, which includes sections on psychosocial factors and issues.)

Basic human needs for self-protection and protection of loved ones can have both positive and negative impacts on public health efforts. Stress, worry, and fear will be present to varying degrees throughout a pandemic. Communications professionals

should work ahead of time with others-including mental health experts-to assess the effect of message content on public anxiety, anticipate other possible stressful situations, and plan appropriate countermeasures.

Additional considerations for developing and disseminating messages and materials about pandemic influenza include the following:

- Assess existing organizational resources for communications, including materials and messages to meet concerns and information needs of target audiences and identify current and potential information gaps.
    - Maintain current, accessible, and secure communications contact lists and databases.
    - Develop a portfolio of communications information sources, including material on topics such as clinical and laboratory diagnostics, infection control practices, isolation and quarantine procedures, stigmatization management, travel control authority, and legal issues related to the pandemic. States and localities will find much information for a portfolio through the www.pandemicflu.gov website and other resources during a pandemic and are encouraged to use or adapt these materials.
        - Work with local subject-matter experts to adapt key national messages about topics such as basic medical treatments, prioritization recommendations for high-risk groups, use of antiviral medications, and access to care. HHS will provide communications materials (e.g., fact sheets, question-and-answer documents, and message maps) for states and localities to use and adapt.
        - Work with local subject-matter experts to adapt communications components of education courses and materials in multiple formats for professional audiences. Consult the www.pandemicflu.gov and www.cdc.gov/flu/ websites for information about specific materials and training opportunities.
- Develop a specific, consistent plan to identify and address rumors and misinformation promptly. Test the plan before a pandemic occurs and modify as needed to ensure it works.
- Identify preferred channels for target audiences. For example, many healthcare providers will have no experience with an influenza pandemic and will rely in part on state and local health departments for rapid access to information.
- Ensure the availability of communications products in multiple languages, based on the demographics of the jurisdiction. Health departments may choose to use or adapt translated materials that will be available on the www.pandemicflu.gov and www.cdc.gov/flu/ websites. Test key messages with local target audiences and revise them as needed. CDC will engage in message and materials testing activities and share the results broadly through websites and via the National Public Health Information Coalition (NPHIC).
- Begin disseminating messages and materials to increase the knowledge and understanding of the public, healthcare professionals, policy-makers, media, and others about unique aspects of pandemic influenza that distinguish it from seasonal influenza, and generally what to expect during different phases of an influenza pandemic.
- Provide coordinated information on ways to access help (e.g., hotlines, helplines) and self-help (e.g., psychological resources, and stress and anxiety management).

S10-IV. RECOMMENDATIONS FOR THE PANDEMIC PERIOD

HHS will coordinate international information exchange and the coordination of messaging through WHO and other international partners, as appropriate. Domestic health communications, including state and local public health communications efforts, should be directed to rapid sharing of appropriate, up-to-date information on what is known and what is unknown about the progression of the outbreak, the possible disruptions to routines and events, and contingency measures. Consistency in messaging across jurisdictions is strongly advised.

The Pandemic Period is likely to last much longer than a typical influenza season and may occur in waves within communities. During this period, watch especially for challenges that may arise with staff fatigue or absenteeism due to illness, difficulties with continuity of services, and problems associated with institutional memory that may occur with high staff turnover. Communications staff and others may need to modify plans made during the Interpandemic and Pandemic Alert Periods.

Primary areas on which communications professionals should focus during the Pandemic Period are providing timely, accurate information in especially challenging conditions, coordinating communications leadership across all tiers of jurisdiction (e.g., local, state, regional, and national), and promptly addressing rumors, misperceptions, stigmatization, and any unrealistic expectations about public and private health provider response capacity.

A. Activating emergency communications plans

Consider the context of the local situation when making decisions to activate formal emergency communication systems at the state and local levels. State and local health departments may want to consider potential thresholds and triggers that might indicate that communications demands are likely to escalate quickly. These might include developments that raise the health risk to local populations (for example, if a human case of avian influenza is reported in a local jurisdiction). As communications demands escalate, state and local health departments may want to activate emergency communications plans, including local toll-free information hotlines and an emergency communications website with links to the www.pandemicflu.gov website.

B. Refining and delivering messages

The following are steps for states and local areas to consider, in collaboration with federal partners:

- Provide regular updates and offer opportunities to address questions (e.g., in partnership with news media, in public forums, and in printed or electronic messages).
- Distribute practical information, such as travelers' advisories, infection control measures, and information about potential priority distribution of antiviral medications and first-generation vaccines. Be prepared to immediately address questions related to initial case(s) and to provide guidance to the public about disease susceptibility, diagnosis, and management, as well as other topics.
- Reinforce and verify ways to help people protect themselves, their families, and others, including self-care information for psychological well-being.
- Address rumors and misinformation promptly and persistently.
- Take steps to minimize stigmatization.

C. Providing timely, accurate information

Depending on health, economic, and overall societal effects, such as the extent of influenza-related illness and death, communications professionals should reassess and adjust as necessary to emerging needs and expectations of public and professional audiences. Areas meriting particular attention include:

- Community subject-matter experts and spokespersons. It may be important to consider additional recruitment and training.
- Effectiveness of procedures for keeping communications lists, materials, and databases current and accurate.
- Open and accessible channels for advice to the public, including ongoing functioning of hotlines in collaboration with the CDC-INFO telephone line. In addition to providing ready access to inquiries and concerns, state and local hotlines can help communications professionals assess community awareness and behaviors and adapt communications strategies.

D. Providing coordinated communications leadership across jurisdictional tiers (e.g., local, regional, state, and national)

- Work with state and local officials to involve communications professionals on senior leadership teams, including roles as liaisons to national communications teams at CDC and other agencies as necessary.
- Maintain strong working relationships with colleagues in other jurisdictions and regions, even when an outbreak may not yet have affected your area directly or may have subsided locally. The following colleagues are especially important to consider.
  - Public affairs directors and information officers from other local and state health departments
  - City and state government public affairs officers
  - Communications staff at congressional and other government offices
  - Communications staff at local and regional police, fire, and emergency management offices
  - Regional health and emergency preparedness colleagues
  - State and local mental health agencies
  - Hospital public relations/affairs departments
  - State and local Emergency Operations Center coordinators
  - Federal Emergency Operations Centers
- Promote public acceptance and support for national response measures and contingency plans.

E. Promptly addressing rumors, misperceptions, stigmatization, and unrealistic expectations about the capacity of public and private health providers

After the initial stages of a pandemic, news media coverage may become more mixed, with both positive and critical coverage. Hero stories may emerge, while "what ifs" and negative images may start to compete for the public attention. As the media proceeds into in-depth analysis of what happened and why, these elements become important to an effective response:

- Monitor news media reports and public inquiries to identify emerging issues, rumors, and misperceptions and respond accordingly.
- Conduct "desk-side briefings" and editorial roundtables with news media decision-makers.
- Proactively address groups that voice overly critical, unrealistic expectations.
- Establish trust with marginalized groups subject to or experiencing stigmatization and cite specific media outlets for inaccurate, misleading, or misguided reporting that may serve to encourage stigmatization.
- Maintain scheduled access to pandemic subject-matter experts to balance the media's needs with other subject-matter expert priorities.

APPENDIX 1. BACKGROUND INFORMATION FOR DEVELOPING COMMUNICATIONS MESSAGES ABOUT PANDEMIC INFLUENZA

The language, timing, and detail of key messages will depend on a number of factors, including demographics and group psychological profiles of intended audiences, available or preferred media, and urgency. However, the following points may help communications professionals adapt appropriate health messages related to an influenza pandemic:

- By definition, pandemic influenza will result from a new influenza A subtype against which humans have limited or no natural immunity. Pandemic influenza virus infection therefore is likely to cause serious, possibly life-threatening disease in greater numbers, even among previously healthy persons, than occurs during seasonal interpandemic influenza outbreaks.
- Global influenza pandemics are unpredictable events, presenting challenges for communication..
- Global and domestic surveillance, coupled with laboratory testing, are vital to identifying new influenza A subtypes virus strains with pandemic potential.
- The threat of a pandemic may be heightened when a highly pathogenic avian influenza A virus spreads widely among birds and infects other animals, including humans. The strains can mutate or adapt and give rise to a strain that spreads easily from person to person in a sustained manner, causing a pandemic.
- Illness and death may be much higher during a pandemic than during annual seasonal community influenza outbreaks; pandemics can also occur in waves over several months.
- It could take many months to develop an effective pandemic influenza vaccine and immunize substantial numbers of people. Antiviral medications for treatment or prevention of pandemic influenza could have an important interim role, but may also be in short supply. Consequently, practical and common sense measures, such as frequent handwashing, covering your mouth and nose while sneezing or coughing, and staying home from work or school if you are ill with influenza-like illness, may be important to help prevent the spread of pandemic influenza.
- Although travel restrictions and isolation and quarantine procedures may limit or slow the spread of pandemic influenza in its earliest stages, these measures are likely to be much less effective once the pandemic is widespread. Alternative population containment measures (e.g., cancellation of public events) may be necessary.
- The United States is preparing for pandemic influenza by:
  - Developing a coordinated national strategy to prepare for and respond to an influenza pandemic
  - Educating healthcare workers about pandemic influenza diagnosis, case management, and infection control practices
  - Refining global and domestic pandemic influenza surveillance systems
  - Developing guidelines for minimizing transmission opportunities in different settings
  - Expanding supplies of antiviral medications in the Strategic National Stockpile and establishing guidelines for their use
  - Developing candidate vaccines and establishing plans for the rapid development, testing, production, and distribution of vaccines that may target specific pandemic influenza strains
  - Developing materials that states and localities can adapt as guidance for use during an influenza pandemic.

APPENDIX 2. SAMPLE MATERIALS

HHS will provide communications materials for states and localities throughout all pandemic phases. Many of these resources will made available at appropriate times on the www.pandemicflu.gov website. Others will be disseminated by using the Health Alert Network (HAN), Epidemic Information Exchange (Epi-X), and other resources for health professionals. The following list offers a sample of the types of communications materials that states and local areas can expect from CDC. This is not an inclusive list and may change depending on the nature and circumstances of a specific influenza pandemic threat. See Appendix 3 (of this supplement for additional resources.

Pandemic Influenza Fact Sheet
http://www.cdc.gov/flu/avian/gen-info/pandemics.htm

Avian Influenza Fact Sheet
http://www.cdc.gov/flu/avian/gen-info/facts.htm

Guidance to Travelers
http://www.cdc.gov/travel/other/avian_flu_ah5n1_031605.htm

Interim Guidance for U.S. Citizens Living Abroad
http://www.cdc.gov/travel/other/avian_flu_ig_americans_abroad_032405.htm

Sample CDC News Conference Transcript
http://www.cdc.gov/od/oc/media/transcripts/t040127.htm

Managing Anxiety in Times of Crisis
http://mentalhealth.samhsa.gov/cmhs/managinganxiety/default.asp

APPENDIX 3. ADDITIONAL RESOURCES

HHS and its agencies will make resources available to state and local health professionals to assist with their communications responsibilities during Interpandemic, Pandemic Alert, and Pandemic Periods. Because information may change frequently, check the www.pandemicflu.gov and www.cdc.gov/flu/ websites for up-to-date materials. Communications professionals in states and local areas will be able to localize and download most resources, including posters, brochures, fact sheets, media kits, webcasts, and archived satellite broadcasts. Much of the material will also be available through e-mail or mail orders. Material will include color and black and white versions for healthcare and public health professionals and for public audiences, as well as specific versions for low-literacy populations. As appropriate and feasible, material will be provided in a variety of languages.

One of the most comprehensive and practical resources for communications professionals is the CDCynergy CD-ROM set produced by CDC. Emergency Risk Communication CDCynergy is applicable to communicating before and during an influenza pandemic. Communications staff also may find the CDCynergy 3.0 disk helpful. Information about CDCynergy is available on CDC's website at http://www.cdc.gov/communication/cdcynergy.htm.

Communicating in a Crisis: Risk Communication Guidelines for Public Officials is available on SAMHSA's website at http://www.riskcommunication.samhsa.gov/index.htm and bound copies can be ordered online at no charge from SAMHSA's National Mental Health Information Center (http://store.mentalhealth.org/publications/ordering.aspx) or by calling 1-800-789-2647. This pocket reference describes basic skills and techniques for clear, effective crisis communications and information dissemination, and provides some of the tools of the trade for media relations.

Other resources

National Vaccine Program Office Pandemic Influenza Website
http://www.HHS.gov/nvpo/pandemics/

WHO Pandemic Influenza Website
http://www.who.int/csr/disease/influenza/pandemic/en/

MMWR Guide for Influenza
http://www.cdc.gov/mmwr/mguide_flu.html

Epidemic Information Exchange (Epi-X)
http://www.cdc.gov/mmwr/epix/epix.html

Health Alert Network (HAN)
http://www.bt.cdc.gov/documentsapp/HAN/han.asp; http://www.phppo.cdc.gov/han

Centers for Public Health Preparedness
www.asph.org/acphp

- This website provides locating information and links to the 40 centers involved in this network. The centers form a unique partnership that includes accredited schools of public health, dentistry schools, medical schools, veterinary schools, and state and local health departments. Together, the partners provide a countrywide defense system through the preparation of front-line public health workers and first responders.

Vaccine-Specific Sites and Resources
Vaccine Adverse Events Reporting System (VAERS) website at http://vaers.hhs.gov/ or call 1-800-822-7967

Surveillance Sites
CDC Influenza Surveillance Data
EISS: European Influenza Surveillance Scheme
EuroGROG: International Influenza Surveillance
World Health Organization (WHO): Flunet

Outbreak Sites
Animal and Plant Health Inspection Service (APHIS), Veterinary Services, U.S. Department of Agriculture (USDA)
APHIS coordinates efforts to prepare for and respond to outbreaks of exotic animal diseases, including highly pathogenic avian influenza. Results of surveillance for influenza A viruses in avian species in the United States are reported each year by the National Veterinary Services Laboratories in the Proceedings of the U.S. Animal Health Association Annual Meeting.

World Health Organization Disease Outbreak Site
The World Health Organization (WHO): disease outbreaks

Research Sites
National Institute of Allergy and Infectious Diseases (NIAID)
http://www.niaid.nih.gov/dmid/influenza/pandemic.htm

USDA Agricultural Research Service
Agricultural Research Service (ARS), USDA
The ARS' Southeast Poultry Research Laboratory publishes information on avian influenza research and contacts for further information.

Manufacture and Licensing of Influenza Vaccine
Center for Biologics Evaluation and Research (CBER), FDA
CBER plays a critical role in the manufacture and licensing of influenza vaccine.

WHO Global Influenza Preparedness Plan
http://www.who.int/csr/resources/publications/influenza/WHO_CDS_CSR_GIP_2005_5/en/index.html

APPENDIX 4. HHS PANDEMIC INFLUENZA RISK COMMUNICATION AND PUBLIC OUTREACH STRATEGY

OVERVIEW

Pandemic influenza risk communication strategies are a critical and necessary component of pandemic influenza preparedness. To be effective, these strategies should be based on scientifically derived risk communications principles and are critical before, during, and after an influenza pandemic. Effective communication guides the public, the news media, health-care providers, and other groups in responding appropriately to outbreak situations and adhering to public health measures.

The main objective of this HHS communication strategy is to prepare the U.S. public and communities for an influenza pandemic by developing messages and materials to share with local, public and private sectors as well as our global partners. In advance of a pandemic, a system can be developed for alerting the public and draft messages and materials can be prepared.

A critical component of national preparedness for an influenza pandemic is informing the public about this potential threat and providing a solid foundation of information upon which future actions can be based. Once a pandemic occurs, our ability to communicate effectively will help HHS manage the public health implications of a pandemic. Studies have shown that the public will respond and cooperate more readily if they are involved directly in discussions and planning for future events. The HHS plan includes both strong risk communication and public outreach in order to build public trust, confidence, and cooperation. For many communities, local leaders may have to rely on risk communication as the primary tool to manage the crisis.

The communication strategy provides HHS guidance on the type of information that is crucial to convey in initial messages in order to prompt appropriate public responses after a crisis situation; the messages that can be delivered prior to, during, and after an incident; the obstacles to effective communications and how they can be minimized; opportunities that currently exist and how to maximize resources; the questions that we can anticipate from the public. This strategy reflects a two year agenda for pandemic preparedness communication and public outreach activities.

Importantly, pandemic influenza risk communication must be approached differently than many other disasters and emergencies. For example, pandemic influenza is likely to be wide-spread (not localized) and will therefore strain National resources. Communities will need to develop local plans for community continuity. In addition, pandemic influenza is likely to be a prolonged event, which will require a plan for ensuring sustained societal functions.

The objectives of this HHS communication strategy are to:

- prepare the U.S. public and communities for a pandemic;
- communicate the need for local preparedness and that Because of t “not business as usual”;
- develop central messages and materials that can be shared broadly;
- coordinate across HHS and other Federal Departments; and
- provide support to our global partners.

GENERAL RISK COMMUNICATION PRINCIPLES

Using sound and thoughtful risk communication strategies can assist public officials in preventing fear-driven, and potentially damaging public responses to crises such as bioterrorism and pandemic disease outbreaks. These strategies can help foster trust and confidence that are vital to public health.(Covello et al., 2001; Maxwell, 1999). Before a crisis occurs, public officials can prepare communities, risk managers, government spokespersons, public health officials, the news media, physicians, and hospital personnel with appropriate messages that can help build public confidence in public officials and the measures they recommend. (O'Toole, 2001).

The HHS National Pandemic Influenza Risk Communications and Public Outreach Strategy follows seven key risk communications concepts.

1. When health risks are uncertain, as likely will be the case during an influenza pandemic, people need information about what is known and unknown, and interim guidance to formulate decisions to help protect their health and the health of others.
2. An influenza pandemic will generate immediate, intense, and sustained demand for information from the public, healthcare providers, policy makers, and news media. Healthcare workers and public health staff may need training in media relations and public health communications.
3. Timely and transparent dissemination of accurate, science-based information about pandemic influenza and the progress of the response can build public trust and confidence, particularly when such communication efforts are guided by established principles of risk communication.
4. Coordination of message development and release of information among federal, state, and local health officials is critical to help avoid confusion that can undermine public trust, raise fear and anxiety, and impede response measures.
5. Guidance to community members about how to protect themselves and their family and colleagues is an essential component of crisis management.
6. Information to public audiences should be technically correct and sufficiently complete to encourage support of policies and official actions without seeming patronizing to the public.
7. Information presented during an influenza pandemic should minimize speculation and avoid over-interpretation of data, overly confident assessments of investigations and control measures, and critical comments related to other jurisdictions.

The two most important concepts relate to communicating uncertainty, openly and honestly acknowledging that "this will not be business as usual."

Recognizing and admitting uncertainty is a component of most risk communication situations (Plough et al., 1988; and Chess, 1989). Scientific uncertainty can complicate communications when officials try to satisfy the public's demand for reliable and meaningful information for many risk situations. Public health officials frequently face the dilemma of having to acknowledge and explain uncertainty to a public that thinks scientific findings are precise, repeatable, and reliable. Moreover, the public often associates correlation and association as being the same as causality. As a result, officials often face the additional task of trying to explain the data's limitations and uncertainties. Audiences need to be provided as much information as possible to help them understand that uncertainty is part of the process and that the answers may change as new information and science becomes available.

Public officials must also acknowledge that a crisis demands an acknowledgment that "this will not be business as usual." This can be communicated by:

- Emphasizing the rationale and importance of adherence to public health measures that some people may consider intrusive (e.g., quarantine).
- Helping to set reasonable expectations of public health and health care systems.
- Promptly address rumors, inaccuracies, and misperceptions.
- Minimizing stigmatization that may occur during a pandemic.
- Ensuring that high-risk groups and others with special needs (e.g., non-English speaking populations, difficult-to-reach communities, and persons living in institutional settings) receive appropriate information.
- Acknowledging the anxiety, distress, and grief that people experience during long-term, major public health crisises such as pandemics.

HHS PANDEMIC INFLUENZA RISK COMMUNICATION AND PUBLIC OUTREACH STRATEGY

During the prepandemic or interpandemic period, national, state, and local communities need to disseminate messages explaining why pandemic influenza is a potential public health threat, what is being done to prepare, how a pandemic would be different from annual influenza outbreaks, and what communities can do in advance. A portfolio of materials, including other sources of information is being developed by HHS for use by communities and other groups. A national website www.pandemicflu.gov will be updated regularly and serve as a national information clearinghouse. Nine key components define the HHS communications strategy:

1) PLANNING AND ASSESSMENT OF CURRENT KNOWLEDGE

- Determine what communications actions will be taken and by whom in advance of a pandemic (i.e. prepandemic) and once a pandemic is confirmed by WHO
- Ascertain communication needs for various audience segments (i.e. What materials, resources, processes, and systems, will be necessary in both phases?)
- Conduct an environmental scan or an assessment of current knowledge of pandemic influenza, which will include:
- Scholarly literature review on Avian Flu or whatever pandemic flu strain is the problem, public health risks, public and political response to similar incidents (e.g., SARS),.
- Review of media coverage of pandemics, Review of web sources
- Assess and analyze media and public baseline knowledge and attitudes.
- Review current national and international efforts and programs to control the pandemic and work with international partners to coordinate activities (WHO)

2) FORMATIVE AUDIENCE RESEARCH

- Define public perceptions, attitudes, beliefs, . Study these from communication perspective to determine how to position information so that people attend to messages and act upon them.
- Conduct 2 sets of 9 cognitive interviews and 16 focus groups with general public.
- Conduct 18 telephone stakeholder interviews with health professionals and community leaders.

3) MESSAGE AND MATERIAL DEVELOPMENT

- Develop prepandemic (WHO intrapandemic and pandemic alert levels) and pandemic messages and materials based on risk communication principles, as outlined in the WHO Outbreak Communication Guidelines.
- Define audiences and develop materials for these audiences.
- Develop message maps and concepts appropriate for each "Phase" of an influenza pandemic development. To test event messages, a video-based scenario will be used to simulate emotional response during a pandemic.
- Coordinate with other agencies to identify pre-event and event material needs and to develop new materials as needed. Materials may include:
    - "HHS Prepares for Pandemic Influenza" - a sixteen page, color version of the pandemic plan for the public that describes the major issues, decisions, actions regarding pandemic influenza.
    - Live announcer copy
    - Core Q&As
    - Hotline response materials

- Fact sheets
- B-roll
- Graphics to support HHS communication (animation)

- Conduct focus groups with general public to pretest event messages separately and/or materials. Provide additional support for material development as needed.

4) CROSS GOVERNMENT COLLABORATION AND COORDINATION

- Establish a cross agency working group that includes communication, policy and subject matter experts. This working group will review and shares strategies and activities being undertaken by each agency and develop a coordinated communication approach. This working group will:
  - Develop consistent messages about pandemic influenza
  - Ensure common understanding of HHS objectives and strategies
  - Leverage existing activities and resources to address pandemic influenza
  - Develop an inventory of current activities
  - Identify gaps and make recommendations on how they can be filled
  - Coordinate media planning, stakeholder outreach
  - Coordinate communications systems as appropriate.
  - Outreach to other Departments in the Federal government and international partners.

5) TRAINING

- Coordinate Training sessions for emergency risk communication among "master trainers" as identified through previous training courses provided by CDC, as well as CDC recommendations. These core trainers would then provide on the ground training within their regions and states focusing specifically on Pandemic Influenza.
- Conduct media training for spokespersons on public health crisis response and risk communications principles.
- Prepare a highly specialized risk communication and message development workshop. This workshop would be focused on building trust across policy makers, communications experts, and subject matter experts across HHS and partner agencies to support effective risk communication during an outbreak of Pandemic Influenza.
- Run a senior official pandemic influenza/communication-focused exercise in cooperation with other government departments.

6) MEDIA OUTREACH

- Coordinate closely with the CDC and other HHS agencies on a National Pandemic Influenza Media Plan , which would include:
- Develop core press materials to serve as backgrounder documents for federal, state and local partners, using existing CDC materials as a starting point
- Conduct media briefing with key national outlets to demonstrate how HHS will function and discuss community planning
- Coordinate media relations with Canada, UK, Mexico, WHO, PAHO, Japan, the EU, and GHSAG, as appropriate.
- Coordinate and host a total of six informational roundtables with:

Key science and health writers/reporters to lay out the groundwork for basic understanding of a pandemic, the risk of an outbreak, the public health response, fact/myths about pandemics, the role of infection control in managing the outbreak, etc.

Key minority media and those representing special-needs groups.

- Review and enhance media lists.

7) COMMUNITY CONTINUITY PLANNING

In collaboration with other government offices (e.g. Department of Education) HHS will develop toolkits specific to different audience segments (e.g. socio-economic considerations) to help inform them about the potential threat of a pandemic, the implications of a pandemic for this sector, and what this sector needs to know in advance so that they can best prepare.

HHS will:

Conduct research into existing infrastructures and plans that can be models for this effort.

Engage community leaders in pre-pandemic planning

- Convene multiple stakeholders meeting.
- Publish proceedings as a document on community continuity planning for Pandemic Influenza and distribute widely including online/electronically
- Develop tool kits for communities for continuity planning working with other governmental partners (e.g. Dept of Education on Tool Kit for Schools)
- Provide exercises/scenarios with leaders' guide on the Pandemic so that communities can use these to determine what they need to put in place, what choices/options they face.
- Develop an online exercise activity designed to help community groups plan for ensuring that community members have access to needed services (e.g., child care, transportation to essential appointments and essential supplies) in a pandemic influenza event. The exercise will be designed similarly to a board game. The outcome for community groups participating in the game will bee to have developed a set of materials such as telephone trees, transportation plans, and community maps marked with the location of essential services, the location of individuals who need assistance, etc. Training will be based on core scenario developed for other trainings.

8) BUSINESS CONTINUITY PLANNING

Stimulate and support business leader continuity planning.

Engage Business Leaders in Pandemic Flu Continuity Planning.

Help them understand nature of the outbreak and why employees should stay home. Provide information on how to plan to continue operations during a pandemic.

Support their exploration of how they can use volunteers to deliver good and services to quarantined community members.

Support their exploration of how they can support public health response

Conduct Business Roundtables

Work with SBA, DOC, DOL and other stakeholders such as Chambers of Commerce, to convene four key business leader and union representatives in a series of roundtables segmented by business size, and/or geography, and/or nature of business.

- Publish outcome of meeting proceedings and widely distribute

- Provide handbook for business leaders and other stakeholders to encourage and support their planning for/coping with Pandemic Influenza. This would include background information on all relevant topics.

9) PUBLIC ENGAGEMENT

Expert Discussions

Host roundtable discussions with medical influencers and opinion leaders Identify and convene key health professional influencers for an "expert discussion" to better understand the likely criticisms the agency may face from the public, and also help these influencers better understand the challenges of pandemic influenza management, relevant research underway, etc. so that they will have a better understanding of what they are commenting on if called upon by the media during an outbreak.

Town Hall Meetings in Six Cities (San Diego, San Francisco or Seattle; Detroit; Miami; Dallas or Fort Worth; Philadelphia and Mobile) Work with Council for Excellence in Government to convene town meetings across the nation with key stakeholders to engage them in planning for pandemic and community continuity.

- public health/public officials
- private sector clinicians
- education sector
- business sector
- non-profit/volunteer sector

Format of town meetings will include a primary session of 200 participants across stakeholder groups, with breakout sessions following. This will include location scouting, panelist research, media and community outreach. Tasks will include:

- secure panelists and sub panelists in the following areas: HHS leadership; local public heath leadership; local private sector clinical officials; local nonprofit/volunteer community; local education community; local business leaders
- publicize event through media partnerships and strategic outreach to build community audience of 200 people
- conduct on-line registration that includes audience pre-event polling
- research on locality and specific issues and concerns for discussion
- secure nationally recognized media personality for moderator and A/V vendor
- produce moderator guide (show script)
- oversee all media relations prior, during and post event
- produce town hall event, including show production, live audience polling and on-site event management
- produce and facilitate post town hall leadership symposium

Public Dialogue Sessions—Meetings with National stakeholder organizations at IOM in July, Sept to discuss priority groups for vaccination during a pandemic. Meetings with local citizens in Atlanta, Omaha, Boston, and Portland in August and September.

10) INTERNATIONAL SUPPORT

- Work with WHO to support public health risk communications needs globally.
- If requested, provide template materials that can be adapted to local needs.
- Support global risk communication training through WHO

HHS RESPONSIBILITIES

Pandemic Period

Develop key messages and materials and conduct audience research and message testing and share results with state and local communications staff.

Provide tools and resources through the www.pandemicflu.gov and other avenues to help educate state and local communications staff.

Identify and train lead spokespersons.

Provide state and local health agencies with guidance about developing communications aspects of preparedness plans.

Work with state and local governments to incorporate communications preparedness as part of larger preparedness exercises.

Work with other non-public health sectors to help provide communications tools for their communities.

Work with the World Health Organization (WHO) and other international public health partners to plan and coordinate communication activities for an influenza pandemic.

Pandemic Alert

Coordinate pandemic influenza media messages to ensure consistency

Provide regular updates about situations that pose potential pandemic influenza threats (e.g., through Health Alert Network [HAN] notices and Web site postings).

Distribute educational messages about pandemic influenza and ways that people can protect themselves and their families

Distribute practical information, such as travel advisories, infection control, availability and use of antiviral medications and vaccines, and specific public health actions that may be needed.

Address rumors and false reports regarding pandemic influenza threats.

Pandemic Period

Coordinate pandemic influenza media messages to ensure consistency

Coordinate communications activities with state and local communications staff, including regional or local communications centers as appropriate.

Promptly respond to rumors and inaccurate information to minimize concern, social disruption, and stigmatization

supplement 11
workforce support: psychosocial considerations and information needs

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SUMMARY OF PUBLIC HEALTH ROLES AND RESPONSIBILITIES IN WORKFORCE SUPPORT

INTERPANDEMIC AND PANDEMIC ALERT PERIODS

Healthcare institutions, state and local health agencies, first-responder organizations, and employers of essential service workers:

- Institutionalize psychosocial support services for employees who participate in or provide support for the response to public health emergencies such as influenza pandemics.
- Prepare educational and training materials on psychosocial issues for distribution to employees during an influenza pandemic.

State and local health departments and other groups:

- Lay the groundwork for the development and implementation of workforce resilience programs to maximize responders' performance and personal resilience during a public health emergency.
- Use behavioral health expertise to develop public health messages, train staff on the use of personal protective equipment (PPE), and conduct other relevant activities.

HHS agencies:

- Create, collect, and provide educational and training materials on psychosocial issues related to pandemic influenza for use by hospital administrators, emergency department staff, safety and security professionals, behavioral health providers, social workers, psychologists, chaplains, and others.
- Provide guidance on the development of self-care strategies and workforce resilience programs.

PANDEMIC PERIOD

Healthcare institutions, state and local health agencies, first-responder organizations, and employers of essential service workers:

- Provide psychological and social support services for employees and their families.
- Address stigmatization issues that might be associated with participation in such services.

Healthcare institutions:

Provide employees with ongoing access to up-to-date information on healthcare and training issues, as well as on the national and local status of the pandemic.

State and local health departments and other groups:

- Implement workforce resilience programs.

HHS agencies:

- Provide medical, public health, and community partners with educational and training materials on psychosocial issues related to pandemic influenza.
- Provide occupational health guidance on psychosocial issues related to the pandemic, including information on anticipated reactions to restrictive public health measures such as quarantine.

S11–I. RATIONALE

The response to an influenza pandemic will pose substantial physical, personal, social, and emotional challenges to healthcare providers, public health officials, and other emergency responders and essential service workers (Box 1). Experience with disaster relief efforts suggests that enhanced workforce support activities can help responders remain effective during emergencies (Appendix 1).

During an influenza pandemic, however, the occupational stresses experienced by healthcare providers and other responders are likely to differ from those faced by relief workers in the aftermath of a natural disaster. Globally and nationally, a pandemic might last for more than a year, while disease outbreaks in local communities may last 5 to 10 weeks. Medical and public health responders and their families will be at personal risk for as long as the pandemic continues in their community. Special planning is therefore needed to ensure that hospitals, public health agencies, first-responder organizations, and employers of essential service workers are prepared to help employees maximize personal resilience and professional performance. An essential part of this planning effort involves the creation of alliances with community-based organizations and nongovernmental organizations with expertise in and resources for psychosocial support services or training.

S11–II. OVERVIEW

Recommendations for the Interpandemic and Pandemic Alert Periods focus on the establishment of psychosocial support services that will help workers manage emotional stress during the response to an influenza pandemic and resolve related personal, professional, and family issues. The recommendations also address the preparation of informational materials for employees and their families and the development of workforce resilience programs to assist families of deployed workers. Recommendations for the Pandemic Period focus on the delivery of psychosocial support services to response workers, provision of occupational health information to healthcare providers, and implementation of workforce resilience programs.

Supplement 11 addresses the psychological and social ("psychosocial") needs of the occupational groups that will participate in the response to an influenza pandemic. These groups include:

- Healthcare workers who provide medical care to ill persons
- Emergency field workers and other public health personnel who help control the spread of infection
- First-responder and nongovernmental organizations whose employees assist affected groups (e.g., persons in quarantine or isolation)
- Essential service workers whose activities maintain normal functions in the community and minimize social disruption
- Family members of all of these groups

Examples of the psychosocial issues faced by these groups and their families are listed in Boxes 1 and 2. Preparedness planning to address these issues will also be useful in responding to other types of public health emergencies. A checklist outlining key workforce support and resource concerns is provided to assist planners (see Appendix 2).

S11–III. RECOMMENDATIONS FOR THE INTERPANDEMIC AND PANDEMIC ALERT PERIODS

A. Institutionalizing psychosocial support services

Healthcare institutions and state and local health agencies should consider incorporating psychosocial support services into ccupational health and emergency preparedness planning for an influenza pandemic. First responders and essential service workers employed by companies and local governments (Box 2) might also benefit from these services. Healthcare and public health planners should also contact community-based organizations and nongovernmental organizations to determine the types of psychological and social support services and training courses available in their jurisdictions.

- Healthcare and public health officials should consider needs for information sharing with emergency planners in schools, law enforcement agencies, and local businesses.
- Planning for the provision of psychosocial support services might include the following activities:
- Ensuring that administrators, managers, and supervisors are familiar with and actively encourage the use of tools and techniques for supporting staff and their families during times of crisis (see S11-IV.A and Appendix 3)
- Training staff in hospitals and occupational health clinics (e.g., social workers, psychiatrists, nurses, psychologists, counselors) in behavioral techniques to help employees cope with grief, stress, exhaustion, anger, and fear during an emergency (see S11-IV.A and Appendix 3)
- If feasible, providing training in psychological support services to persons who are not behavioral health professionals (e.g., primary-care clinicians, emergency department staff, medical/surgical staff, safety and security personnel, behavioral health staff, chaplains, community leaders, staff of cultural and faith-based organizations)
- Identifying additional resources that can be available to employees and their families during and after a pandemic
- Developing strategies to assist staff who have child-care or elder-care responsibilities or other special needs that might affect their ability to work during a pandemic

B. Preparing workforce support materials

Employers of response workers and providers of essential services should obtain or prepare workforce support materials (in hard copy or electronic format) for distribution during a pandemic. These materials should be designed to do the following:

- Educate and inform employees about emotional responses they might experience or observe in their colleagues and families (including children) during an influenza pandemic and about techniques for coping with these emotions (see Appendix 3).
- Educate employees about the importance of developing "family communication plans" so that family members can maintain contact during an emergency.
- Describe workforce support services that will be available during an emergency, including confidential behavioral health services and employee assistance programs.
- Answer questions about infection control practices to prevent the spread of pandemic influenza in the workplace (see **Supplement 4**) and employment issues related to illness, sick pay, staff rotation, and family concerns.

Healthcare institutions should be prepared to provide materials that address healthcare and training issues related to pandemic influenza (see S11-IV.B). To support these efforts, CDC, HRSA, NIH, and SAMHSA will collaborate with the Department of Homeland Security, other federal agencies, and nongovernmental organizations to identify or develop educational materials on:

- Stressors related to pandemic influenza
- Signs of distress
- Traumatic grief
- Psychosocial aspects related to management of mass fatalities
- Stress management and coping strategies
- Strategies for building and sustaining personal resilience
- Behavioral and psychological support resources
- Strategies for helping children and families in times of crisis
- Strategies for working with highly agitated patients

C. Developing workforce resilience programs

State and local health agencies should consider establishing workforce resilience programs that will help deployed workers prepare for, cope with, and recover from the social and psychological challenges of emergency field work. CDC has used this approach with staff members who participated in the tsunami relief effort in 2004-2005 and the Marburg hemorrhagic fever outbreak in Angola in 2005.

To prepare for implementation of workforce resilience programs to cope with the special challenges posed by an influenza pandemic, agencies should do the following:

- Plan for a long response (i.e., more than 1 year).
- Identify pre-deployment briefing materials.
- Augment employee assistance programs with social support services for the families of deployed workers (see S11-IV.C).
- Provide program administrators and counselors with information on:
- Cognitive, physiological, behavioral, and emotional symptoms that might be exhibited by patients and their families (especially children), including symptoms that might indicate severe mental disturbance
- Self-care in the field (i.e., actions to safeguard physical and emotional health and maintain a sense of control and self-efficacy)
- Cultural (e.g., professional, educational, geographic, ethnic) differences that can affect communication
- Potential impact of a pandemic on special populations (e.g., children, ethnic or cultural groups, the elderly).

S11-IV. RECOMMENDATIONS FOR THE PANDEMIC PERIOD

A. Delivering psychosocial support services

Healthcare facilities and public health agencies—as well as companies and local governments that employ essential service providers—should make full use of public health techniques and communication tools that can help response workers manage emotional stress and family issues and build coping skills and resilience. These tools can include:

- Stress control/resilience teams. These teams can assist and support employees and foster cohesion and morale by:
  - Monitoring employee health and well-being (in collaboration with occupational health clinics, if possible)
  - Staffing "rest and recuperation sites" (see below)
  - Distributing informational materials (see S11-III.B).

  Stress control teams in hospitals should observe recommended infection control precautions.
- Rest and recuperation sites. Sites can be stocked with healthy snacks and relaxation materials (e.g., music, relaxation tapes, movies), as well as pamphlets or notices about workforce support services.
- Confidential telephone support lines staffed by behavioral health professionals
- Services for families. Services to families of employees who work in the field, work long hours, and/or remain in hospitals or other workplaces overnight might include:
  - Help with elder care and child care
  - Help with other issues related to the care or well-being of children
  - Provision of cell phone or wireless communication devices to allow regular communication among family members (see S11-III.B)
  - Provision of information via websites or hotlines
  - Access to expert advice and answers to questions about disease control measures and self care.

- Information for commuters. Workers might need alternative transportation and scheduling (e.g., carpooling, employer-provided private transportation, alternate work schedules during off-peak hours) to avoid exposure to large groups of potentially infected persons.
- Services provided by community- and faith-based organizations. Activities of these organizations can provide relaxation and comfort during trying and stressful times.

A list of additional resources is provided in Appendix 3.

B. Providing information to responders

1. Healthcare providers

Healthcare providers—especially those who work in hospitals—are likely to be under extreme stress during a pandemic (see Box 3) and will have special needs for open lines of communication with employers and access to up-to-date information. Healthcare facilities should ensure that employees have ongoing access to information on the following:

- International, national, and local progress of the pandemic
- Work issues related to illness, sick pay, staff rotation, shift coverage, overtime pay, use of benefit time, transportation, and use of cellphones
- Family issues, especially availability of child care
- Healthcare issues such as availability of vaccines, antiviral drugs, and personal protective equipment (PPE); actions to address understaffing or depletion of PPE and medical supplies; infection control practices as conditions change; approaches to ensure patients' adherence to medical and public health measures without causing undue anxiety or alarm; management of agitated or desperate persons; guidance on distinguishing between psychiatric disorders and common reactions to stress and trauma; management of those who fear they may be infected, but are not (so-called "worried well"); and guidance and psychosocial support for persons exposed to large numbers of influenza cases and deaths and to persons with unusual or disturbing disease symptoms.
- Because healthcare workers might be called upon to fill in for sick colleagues and perform unfamiliar tasks, healthcare facilities should consider providing written instructions for "just-in-time" cross training on essential tasks.

2. Other occupational groups

Other occupational groups that might participate in the response to pandemic influenza (including police, firefighters, and community outreach workers) should receive training materials that will help them anticipate behavioral reactions to public health measures such as movement restrictions (e.g., quarantine, isolation, closure of national or regional borders), especially if such actions are compounded by an economic crisis or abrupt loss of essential supplies and services.

3. Stigmatization issues

Healthcare workers and other emergency responders should be provided with information on what to do if they or their children or other family members experience stigmatization or discrimination because of their role in the pandemic influenza response. Hospital public affairs offices should be prepared to address these issues without delay.

C. Implementing workforce resilience programs

During an influenza pandemic, state and local health agencies should consider implementing workforce resilience programs that meet the special needs of deployed workers—including workers who do not change job site but whose assignments shift to respond to the pandemic—and the central operations personnel who support them around the clock. First-responder or nongovernmental organizations that send employees or volunteers to assist patients at home or in hospitals might establish similar programs. Workforce resilience programs could provide the following services:

1. Predeployment/assignment

- Conduct briefings and training on behavioral health, resilience, stress management issues, and coping skills.
- Train supervisors in strategies for maintaining a supportive work environment.

2. During deployment/assignment

- To support responders in the field:
  - Deploy several persons as a team and/or assign "buddies" to maintain frequent contact and provide mutual help in coping with daily stresses.
  - Frequently monitor the occupational safety, health, and psychological well-being of deployed staff.
  - Provide access to activities that help reduce stress (e.g., rest, hot showers, nutritious snacks, light exercise).
  - Provide behavioral health services, as requested.
- For central operations personnel:
  - Enlist stress control or resilience teams to monitor employees' occupational safety, health, and psychological well-being (see S11-IV.A).
  - Establish rest and recuperation sites (see S11-IVA), and encourage their use.
  - Provide behavioral health services, as requested.
- For families of responders:
  - Provide all of the services listed under "Services for Families" in S11-III.A (Note: Services for Families not listed in S11-III.A)
  - Enlist employee assistance programs to provide family members with instrumental support (e.g., assistance obtaining food and medicine) and psychosocial support (e.g., family support groups, bereavement counseling, and courses on resilience, coping skills, and stress management).
  - Provide a suggestion box for input via e-mail or anonymous voice-mail with a toll-free number.
  - Continue to provide outreach to employees' families to address ongoing psychological and social issues.

Throughout the response, policies on personnel health and safety should be reviewed and revised, as needed.

3. Post-deployment/assignment

- Interview responders and family members (including children) to assess lessons learned that might be applied to future emergency response efforts (see Box 4).
- Provide ongoing access to post-emergency psychosocial support services for responders and their families (on-site or through partner organizations).
- Conduct an ongoing evaluation of the after-effects of the pandemic on employees' health, morale, and productivity.

BOX 1. PSYCHOSOCIAL ISSUES FOR RESPONSE WORKERS

Psychosocial issues that response workers might need to address include:

- Illness and death among colleagues and family members
- Fear of contagion and/or of transmitting disease to others
- Shock, numbness, confusion, or disbelief; extreme sadness, grief, anger, or guilt; exhaustion; frustration
- Sense of ineffectiveness and powerlessness
- Difficulty maintaining self-care activities (e.g., getting sufficient rest)
- Prolonged separation from family
- Concern about children and other family members
- Constant stress and pressure to keep performing
- Domestic pressures caused by school closures, disruptions in day care, or family illness
- Stress of working with sick or agitated persons and their families and/or with communities under quarantine restrictions
- Concern about receiving vaccines and/or antiviral drugs before other persons

These issues may be exacerbated by:

- Lack of information
- Rumors, misconceptions, or conspiracy theories
- Loss of faith in health institutions, employers, or government leaders
- Belief that medical resources are not available or fairly distributed
- Death of immediate supervisors or other leaders in the response effort
- Mass casualties and deaths among children
- Economic collapse or acute shortages of food, water, electricity, or other essential services
- Restrictions on civil liberties that are perceived to be inequitable
- Infection control procedures that limit personal contact or hinder communications

Psychosocial issues related to the general public are addressed in **Supplement 10.**

BOX 2. PSYCHOSOCIAL ISSUES FOR FAMILIES OF RESPONSE WORKERS

The families of responders will face many challenges in addition to the fears and disruptions that everyone will face during a pandemic. For example:

- Responders might be frustrated, tired, worried, irritable, argumentative, restless, emotional, or distressed.
- Responders might be impatient and less understanding, energetic, optimistic, good natured, or helpful than usual.
- Increased emergency work loads (which might be exacerbated by staffing shortages) can make it difficult for responders to communicate regularly with family members.
- Family members might experience stigmatization or discrimination.

BOX 3. IMPACT OF PANDEMIC INFLUENZA ON HEALTHCARE WORKERS

In addition to the issues faced by all response workers (Box 1), healthcare workers may experience:

- Increased risk of exposure to pandemic influenza
- Constant need to take special precautions to avoid exposure to the pandemic virus
- Illness and death among patients, as well as among colleagues and family members
- Stigmatization and discrimination associated with being perceived as a source of contagion
- Ethical dilemmas, such as conflicts between one's roles as healthcare provider and parent/spouse, or concern about receiving vaccines or antiviral drugs before other people
- Increased difficulty in performing crucial tasks and functions as the number of severely ill patients increases, the healthcare staff decreases, and medical and infection control resources are depleted
- Frustration regarding the need/expectation to maintain business as usual
- Physical isolation associated with use of infection control measures that limit interpersonal contact

Psychosocial issues related to hospital workers are also addressed in **Supplement 3.**

BOX 4. LESSONS LEARNED DURING THE 2004-2005 TSUNAMI RELIEF EFFORT

- It is difficult to prepare responders for everything they might encounter.
- Even seasoned responders can face situations and issues that cause uneasiness and distress.
- It is not unusual for responders to be asked to work outside their areas of expertise.
- Concerns about family and friends rank high on responders' lists of priorities.
- Timely, accurate, and candid information should be shared to facilitate decision-making.
- Self-help activities are essential to mission completion.
- Everything possible should be done to safeguard responders' physical and emotional health.
- Responders do not need to face response challenges alone. They may share their experiences with buddies, teammates, family members, and colleagues.
- It is especially difficult for responders to maintain personal resilience when they witness the deaths of children.
- Organizational differences among groups of responders and cultural differences between victims and responders can impede the timely and efficient provision of emergency services.

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APPENDIX 2. CHECKLIST FOR WORKFORCE SUPPORT SERVICES/RESOURCES

A. Checklist for Interpandemic and Pandemic Alert Periods

Include psychosocial issues in planning

- ❑ Incorporate psychosocial support services into emergency preparedness planning for an influenza pandemic.
- ❑ Coordinate with business, corporations and other private sector interests in planning for behavioral health response and consequences.
- ❑ Develop plans to prepare and support emergency service responders (e.g., police, fire, hospital emergency department staff, mortuary workers) during and following deployment.
- ❑ Prepare for a significant surge of individuals who fear they may be infected, but aren't, who may present at emergency departments or other healthcare locations, or contact health information hotlines.
- ❑ Develop a demographic picture of the community (e.g., ethnic, racial, and religious groups; most vulnerable; special needs; language minorities) and plan for how they might be reached in a disaster.
- ❑ Identify rest and recuperation sites for responders. These sites can be stocked with healthy snacks and relaxation materials (e.g., music, relaxation tapes, movies), as well as pamphlets or notices about workforce support services.
- ❑ Develop confidential telephone support lines to be staffed by behavioral health professionals.
- ❑ Use behavioral health expertise to develop public health messages, train staff on the psychological impact of the use of personal protective equipment (PPE), and conduct other relevant activities.

Identify and access existing resources

- ❑ Work with community-based organizations and nongovernmental organizations to determine the types of psychological and social support services and training courses available in their jurisdictions.
- ❑ Establish public-sector links with private mental health resources such as Red Cross and other national voluntary organizations active in disasters.
- ❑ Develop a plan to manage offers of assistance and invited/uninvited volunteers.
- ❑ Identify gaps, such as culturally competent and multilingual providers, that might affect disaster services.

Train behavioral health and related professionals in disaster response strategies

- ❑ Train behavioral health staff in hospitals, clinics, and related agencies in techniques to help people cope with grief, stress, exhaustion, anger, and fear during an emergency.
- ❑ Train nonbehavioral health professionals (e.g., primary-care clinicians, safety and security personnel, community leaders, and staff of cultural- and faith-based organizations) in basic psychological support services.
- ❑ Establish links to health and medical entities for purposes of assisting in screening potential victims for mental disorders and psychogenic symptomatology, functional impairment, substance abuse, etc.

Develop resources and materials

- ❑ Prepare educational and training materials on psychosocial issues for distribution to workers during an influenza pandemic.

B. Checklist for Pandemic Period

During the first 4 weeks

- ❑ Meet basic needs such as food, shelter, and clothing.
- ❑ Provide basic psychological support (psychological first aid).
- ❑ Provide needs assessments.
- ❑ Monitor the recovery environment (conducting surveillance).
- ❑ Provide outreach and information dissemination.
- ❑ Provide technical assistance, consultation, and training.
- ❑ Foster resilience, coping, and recovery.
- ❑ Provide triage.
- ❑ Provide treatment.
- ❑ Provide psychological and social support services for employees and their families.
- ❑ Address stigmatization issues that might be associated with participation in such services.
- ❑ Implement workforce resilience programs.
- ❑ Work with communications experts to shape messages that reduce the psychological impact of the pandemic.
- ❑ Provide medical, public health, and community partners with educational and training materials.

During subsequent weeks

- ❑ Provide continued outreach, triage, and services.
- ❑ Monitor workforce for signs of chronic or severe psychological distress.
- ❑ Provide assistance in reintegration for workers who were deployed or isolated from work and family.

APPENDIX 3. PSYCHOLOGICAL FIRST AID FOR EMERGENCY RESPONDERS

Along with increased efforts to institutionalize workforce services that support the emotional well-being of responders—both during and after an emergency–a consensus is growing on the usefulness of a set of psychosocial tools and techniques for providing "psychological first aid." The organizations listed below provide information for those interested in learning more about this topic.

- American Psychiatric Association
  www.psych.org/disasterpsych/links/weblinks.cfm
- American Psychological Association (APA) Help Center
  www.apahelpcenter.org
- Disaster Epidemiology Emergency Preparedness (DEEP) Center, University of Miami Miller School of Medicine
  www.deep.med.miami.edu
- National Center for PTSD, Department of Veterans' Affairs
  www.ncptsd.va.gov/
- National Child Traumatic Stress Network
  www.nctsnet.org
- Project Liberty
  www.projectliberty.state.ny.us/

Resources from HHS agencies include:

- CDC/American Red Cross. Maintaining a healthy state of mind
  http://www.redcross.org/preparedness/cdc_english/health.asp
- National Institute of Mental Health (NIMH/NIH/HHS)
  Mental Health and Mass Violence: Evidence-Based Early Psychological Intervention for Victims/Survivors of Mass Violence: A Workshop to Reach Consensus on Best Practices. NIH Publication No. 02-5138, Washington, D.C., U.S. Government Printing Office. 2002
- Substance Abuse and Mental Health Services Administration (SAMSHA/HHS)
  Disaster Readiness and Response
  www.samhsa.gov/Matrix/matrix_disaster.aspx

  Disaster Technical Assistance Center. Research listings and fact sheets on self-care
  www.mentalhealth.samhsa.gov/dtac/Selfcare.asp

  Center for Mental Health Services
  Mental Health Response to Mass Violence and Terrorism: A Training Manual. HHS Pub. No. SMA 3959. Rockville (MD); 2004
  Guide to Managing Stress in Crisis Response Professions (under development).

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